HEMORRHAGE
AND TRANSFUSION

HEMORRHAGE AND TRANSFUSION

AN EXPERIMENTAL AND CLINICAL RESEARCH

BY

GEORGE W. CRILE, A.M., M.D.

PROFESSOR OF CLINICAL SURGERY, WESTERN RESERVE MEDICAL COLLEGE; VISITING SURGEON TO THE PRIVATE WARD SERVICE OF LAKE SIDE HOSPITAL, CLEVELAND, OHIO

NEW YORK AND LONDON
D. APPLETON AND COMPANY
1909

PRINTED AT THE APPLETON PRESS,
NEW YORK, U. S. A.

PREFACE

The material for this research has been obtained during a period of eleven years. The large amount of work required to accumulate the necessary data was accomplished only through the assistance of a number of colleagues whose enthusiasm and delightful companionship mitigated the disappointments and exalted the successes. These men made this work possible, and if it contains any merit, their names deserve a share of the title page.

Dr. D. H. Dolley worked especially on the subjects of hemorrhage and resuscitation, and we conjointly published the results under the titles "Clinical and Experimental Observations on Surgical Hemorrhage" and "An Experimental Research into the Resuscitation of Dogs Killed by Anesthetics and Asphyxia."

Dr. C. H. Lenhart published with me "The Treatment of Illuminating Gas Poisoning," and Dr. H. P. Cole "Transfusion after Bilateral Nephrectomy in Dogs." Dr. D. A. Prendergast and Dr. A. B. Eisenbrey did much of the work on shock. To Miss O. M. Lewis and Dr. A. M. Tweedie I desire to make acknowledgment for their work on hemolysis.

To Dr. J. J. R. Mcleod, Professor of Physiology in Western Reserve University Medical Department, I am under obligations for valuable advice on many of the problems in

physiology which came under consideration, while to Dr. Alexis Carrel my special thanks are due for his kindness in demonstrating the technic of vessel sutures.

In the clinical field I have the opportunity of adding one more to the many previous acknowledgments of indebtedness to my associate, Dr. W. E. Lower, for his advice and assistance, and for the use of his clinical material.

To Dr. H. G. Sloan, Resident, and Drs. G. K. Gamble, A. B. Eisenbrey, L. A. Pomeroy, and A. M. Tweedie, members of the Staff of the Private Ward Service of Lakeside Hospital, I am under many obligations for assistance and for clinical data. To the Resident Staff of St. Alexis Hospital my thanks are also due for similar services.

Dr. F. W. Hitchings did all the preliminary work in perfecting the transfusion cannulæ, besides being, with Dr. R. N. Birge, the first to use the cannula method in performing a clinical transfusion. He has had entire charge of the arrangement of the material in book form. For his many valuable suggestions and criticisms, and for his infinite pains in all the details in his large share of this work, I take particular pleasure in making my grateful acknowledgment.

G. W. C.

TABLE OF CONTENTS

PART I

HEMORRHAGE

PART II

TRANSFUSION

LIST OF ILLUSTRATIONS

PART I

HEMORRHAGE

INTRODUCTION

In the experimental work on animals no experiment was performed in which the particular animal used was not reduced to complete insensibility by means of ether or some other equally efficient anesthetic. If the statement is made that the anesthesia was stopped during an experiment it does not mean that the animal could suffer pain, but that death was threatened from too much anesthetic, more being given as soon as signs of revival were shown. In every experiment in which necessary mutilation was performed the animal was killed before coming out of the anesthetic. Therefore absolutely no suffering was undergone. Very few recovery experiments were performed—no more than were necessary to prove a given fact to the satisfaction of the experimenter. It should be remembered that aside from humanitarian considerations, the recovery animals had to be treated as carefully as patients would have been treated under the same circumstances in order to secure freedom from sepsis and successful results, and that they underwent little or less discomfort than patients would have undergone under similar circumstances. These remarks apply equally to Parts I and II of this book.

Whenever possible tracings were made in each experiment, and in all of the experiments careful notes were taken. Only enough tracings are reproduced to illustrate the points under discussion. This volume is to be regarded as a clinical and experimental study, and not as a handbook.

EXPERIMENTAL STUDIES

CHAPTER I

THE GENERAL PHENOMENA AND TREATMENT OF ACUTE HEMORRHAGE

In collaboration with Dr. D. H. Dolley

PROTOCOLS OF EXPERIMENTS

EXPERIMENT 1

Hemorrhage

August 16, 1904.

Spaniel bitch; weight, 10.9 kilos; condition, good. Ether anesthesia through tracheal cannula. Cannula in right carotid artery connecting with mercury manometer. Cannula for bleeding in left femoral artery. Blood-pressure recorded on kymograph.

3.33.—Control on kymograph drum. Blood-pressure, 140 mm.

3.40.—Began to bleed the animal.

3.45.—Stopped bleeding. 425 c.c. of blood were removed. Blood-pressure, 12 mm. The dog died.

Summary.—The rapid loss of approximately more than one half the total amount of blood was not followed by efficient compensation by the vasomotor system, and death occurred.

EXPERIMENT 2

Hemorrhage

September 3, 1904.

Bull terrier; weight, 13.7 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.08.—Control on drum. Blood-pressure, 146 mm. An accidental loss of 25 c.c. of blood was incurred.

10.15.—Blood-pressure, 146 mm. The femoral cannula was adjusted.

10.23.—Blood-pressure, 136 mm. Began to bleed the animal.

10.45.—375 c.c. of blood were removed (at the rate of 100 c.c. in five minutes). Blood-pressure, 76 mm.

11.21.—Control. Blood-pressure, 124 mm. Began to bleed again.

11.29.—100 c.c. of blood removed.

11.39.—Control. Blood-pressure, 85 mm.

12.01.—100 c.c. of blood removed (total amount, 600 c.c.).

12.03.—Control. Blood-pressure, 60 mm. On burning a paw there was a rise of pressure of 10 mm.

12.20.—Stimulation of the sciatic nerve resulted in a rise of the systolic pressure which was followed by a fall of both the systolic and the diastolic pressure. Blood-pressure, 78 mm.

12.30.—Blood-pressure, 79 mm.

12.36.—Control. Blood-pressure, 90 mm. 80 c.c. more of blood were removed (total, 680 c.c.).

12.42.—Blood-pressure, 58 mm.

12.52.—Burning a paw produced no effect.

12.53.—On stimulating the sciatic nerve no effect was noted.

12.58.—Blood-pressure, 48 mm.

12.58½.—Respiratory failure occurred, and artificial respiration was begun, but death occurred before other measures could be employed.

Summary.—(1) A hemorrhage of about one tenth the total amount of blood was entirely compensated for. (2) A hemorrhage of about three fifths the total amount of blood was fatal in about twenty-five minutes after stopping the hemorrhage. (3) In a hemorrhage of about three fifths the total amount of blood, after compensatory efforts had been dissipated following further bleeding, peripheral stimulation gave no reaction in about fifty minutes, and but slight reaction in twenty minutes.

EXPERIMENT 3

Hemorrhage

August 24, 1904.

Yellow terrier; weight, 8.5 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

2.40.—Control on drum. Blood-pressure, 160 mm.

2.45.—Began to bleed. 100 c.c. removed. Blood-pressure, 116 mm.; 100 c.c.—90 mm.

2.53.—75 c.c. of blood removed (total amount, 275 c.c.). Blood-pressure, 60 mm. Artificial respiration used. Death occurred apparently from the ether.

Summary.—The same as in Experiment 7, q.v.

EXPERIMENT 4

Hemorrhage; Normal Saline Infusion

September 6, 1904.

Black mongrel; weight, 26.3 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.45.—Blood-pressure, 128 mm. Began to bleed.

10.50.—125 c.c. blood removed.

10.54.—100 c.c. blood removed.

11.00.—100 c.c. blood removed.

11.05.—100 c.c. blood removed.

11.12.—100 c.c. blood removed.

11.18.—100 c.c. blood removed.

11.26.—100 c.c. blood removed.

11.32.—100 c.c. blood removed.

11.35.—120 c.c. blood removed.

11.45.—Control. Blood-pressure, 106 mm. On burning a paw there was a rise of pressure of 8 mm. followed by a temporary fall.

11.49.—Blood-pressure, 114 mm.

12.28¾.—Control. Blood-pressure, 110 mm.

12.29.—On burning a paw there was no effect.

12.30.—Stopped the drum.

12.38.—The sciatic nerve was exposed. Blood-pressure, 94 mm.

12.39.—Stimulated the sciatic nerve. There was a fall of 24 mm. with partial recovery to former level.

12.42.—Blood-pressure, 94 mm. The former level was gradually reached.

12.44.—Blood-pressure, 100 mm.

12.49.—Began to bleed again.

12.55.—100 c.c. blood removed.

1.00.—100 c.c. blood removed.

1.01.—Control. Blood-pressure, 74 mm.

1.09.—Control. Blood-pressure, 75 mm. Began to bleed.

1.15.—Control. 100 c.c. blood removed (total amount, 1,245 c.c.). Blood-pressure, 52 mm.

1.26.—Blood-pressure, 48 mm.

1.26½.—On burning a paw there was no effect.

1.27.—The sciatic nerve was stimulated. Muscular contractions followed, and a rise of blood-pressure of 5 mm.

1.28.—On burning a paw there was a barely perceptible rise in the pressure.

1.29.—The sciatic nerve was stimulated. Muscular contractions followed, and a rise of pressure of 2 mm.

1.30½.—Blood-pressure, 42 mm. Laryngeal manipulation was followed by respiratory inhibition. The blood-pressure stayed at the same level.

1.32½.—The above was repeated with the same effect.

1.33.—The sciatic nerve was stimulated, with a slight rise in the pressure following.

1.34.—Began to inject normal saline solution intravenously. Blood-pressure, 39 mm.

1.35.—Stopped giving the ether. 50 c.c. saline solution given.

1.37.—Stopped the drum. Blood-pressure, 44 mm. 50 c.c. saline solution given.

1.38.—Blood-pressure, 48 mm. Gave the ether again.

1.39.—50 c.c. saline solution given.

1.40.—50 c.c. saline solution given.

1.42.—50 c.c. saline solution given.

1.44.—50 c.c. saline solution given.

1.45.—50 c.c. saline solution given.

1.47.—50 c.c. saline solution given.

1.49.—50 c.c. saline solution given.

1.51.—50 c.c. saline solution given. Blood-pressure, 56 mm.

1.57.—Blood-pressure, 50 mm.

2.01.—50 c.c. saline solution given (total amount, 550 c.c.).

2.02.—Blood-pressure, 38 mm. Respiratory failure occurred. Cardiac collapse. On giving 50 c.c. 1–50,000 adrenalin chlorid solution, and performing artificial respiration, there was cardiac failure before the adrenalin was all injected.

Summary.—(1) In a dog with low initial blood-pressure a hemorrhage of about two fifths the total amount of blood produced a fall of only one sixth of the initial height, and reaction to peripheral stimulation disappeared entirely in thirty minutes, while stimulation of the sciatic nerve gave a further depressor effect. (2) Further hemor-

rhage to about three fifths the total amount of blood was much more effectual in lowering the blood-pressure. (3) A short time after profound hemorrhage, laryngeal manipulation produced respiratory inhibition, but no further fall in blood-pressure. (4) Normal saline infusion at the rate of 100 c.c. in two minutes started one and three quarter hours after the bulk of the hemorrhage had occurred, raised the blood-pressure only one fifth of its original height, and was followed by respiratory failure and cardiac failure before one half the amount of blood withdrawn was replaced by it.

EXPERIMENT 5

Hemorrhage; Normal Saline Infusion

SEPTEMBER 1, 1904.

Mongrel bitch; weight, 4 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

4.20.—Control on drum.

4.22.—Respiratory failure occurred, and artificial respiration was used.

4.37.—Control. Blood-pressure, 164 mm. Began to bleed.

4.39.—155 c.c. blood removed. Cardiac and respiratory failure occurred. Blood-pressure, 20 mm. 100 c.c. of normal saline solution were given intravenously at a rapid rate—the first 50 c.c. at the rate of 4 c.c. per minute.

4.50.—Stopped the saline infusion. Blood-pressure (maximum), 142 mm.

4.58.—Control. Magnesium sulphate solution from the manometer was forced into the circulation. The blood-pressure fell to 70 mm. and respiratory spasms occurred.

5.02.—A paw was burned, with very slight reaction. Stopping the artificial respiration momentarily caused a very sharp rise in the blood-pressure.

5.15.—Blood-pressure, 84 mm. The artificial respiration was stopped, and the breathing stopped spontaneously. There was a clot in the cannula leading from the carotid artery to the manometer.

5.30.—Respiratory failure occurred. Artificial respiration was used again, and the heart was massaged, with recovery. Blood-pressure, 66 mm.

5.38.—The dog was killed.

Summary.—(1) Bleeding the dog about one half the total amount of blood produced cardiac and respiratory failure, and on immediately

infusing normal saline solution in amount equal to the amount of blood lost (the first two thirds was given rapidly, and the remaining one third slowly) the blood-pressure was raised to a point seven eighths as high as the original. (2) Twenty minutes after stopping the hemorrhage (there was no compensation) the blood-pressure was raised as high as possible with infusion of normal saline solution, but on burning a paw there was only a slight reaction.

EXPERIMENT 6

Hemorrhage; Normal Saline Infusion

AUGUST, 1904.

Mongrel bitch; weight, 6.9 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

3.00.—Control on drum. Blood-pressure, 134 mm.

3.05.—Respiratory failure was overcome with artificial respiration.

3.10.—Began to bleed slowly by drops. Blood-pressure, 134 mm.

3.40.—105 c.c. blood removed. Blood-pressure, 86 mm.

3.55.—100 c.c. blood removed (total amount, 205 c.c.). Blood-pressure, 64 mm.

4.39.—Blood-pressure, 42 mm. 150 c.c. of normal saline solution were given rapidly intravenously, 50 c.c. of it at the rate of 2 c.c. per minute. There was marked improvement in the heart action and the respiration.

4.58.—Control. Blood-pressure, 60 mm.

5.02.—Burned a paw. A rise of pressure of 4 mm. resulted.

5.05.—Blood-pressure, 50 mm.

5.11.—Control.

5.16.—Blood-pressure, 44 mm. Heart action and respiration good. Saline infusion begun.

5.17½.—Saline infusion stopped.

5.18½.—Saline infusion begun again.

5.20.—Blood-pressure slowly rising. Heart action and respiration good.

5.23½.—More saline solution given in two minutes.

5.32.—Control. Blood-pressure, 54 mm. The dog was then killed.

Summary.—After a wait of forty-five minutes an amount of normal saline solution equal to two thirds of the amount of blood removed was given intravenously, the first part rapidly and the last part slowly. This acted excellently on the heart and respiration, but

the blood-pressure began to fall before the solution was all given, and the subsequent infusion of the same amount in small portions at different intervals raised the pressure but slightly, although there was not the same degree of embarrassment of heart and respiration, and the splanchnic engorgement which was noted when the solution was given all at once.

EXPERIMENT 7

Hemorrhage; Normal Saline Infusion

August 23, 1904.

Spaniel bitch; weight, 8 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

1.45.—Control on drum. Blood-pressure, 130 mm.

1.50.—Began to bleed. After bleeding 100 c.c. slowly, the blood-pressure fell to 86 mm. 200 c.c. blood removed. Blood-pressure, 66 mm. 265 c.c. in all removed. Blood-pressure, 58 mm. Respiratory failure occurring, artificial respiration was used, and 50 c.c. normal saline solution were given intravenously, but death occurred.

Summary.—The fall of blood-pressure was slightly irregular, and more marked during the fairly rapid removal (100 c.c. in three minutes) of the first third of the blood.

EXPERIMENT 8

Hemorrhage; Normal Saline Infusion

September 15, 1904.

Mongrel; weight, 6.3 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

2.50.—Control on drum. Blood-pressure, 140 mm.

2.56.—An accidental hemorrhage of 25 c.c. occurred. Blood-pressure, 122 mm.

2.58.—100 c.c. blood removed. Blood-pressure, 94 mm.

3.00.—100 c.c. blood removed. Blood-pressure, 54 mm.

3.04.—85 c.c. blood removed (total amount, 310 c.c.). Blood-pressure, 34 mm. Artificial respiration begun.

3.06.—Began to inject normal saline solution intravenously.

3.15.—350 c.c. saline solution injected. Blood-pressure, 115 mm. Artificial respiration stopped. The respiration was labored and the dog was partly asphyxiated.

3.16.—Artificial respiration was resumed. Blood-pressure, 88 mm.

3.19.—Stopped the drum. Blood-pressure, 106 mm. Heart action and respiration good.

3.20.—Blood-pressure, 100 mm.

3.20½.—Saline infusion begun again.

3.22.—50 c.c. saline solution given. Blood-pressure, 113 mm.

3.24.—50 c.c. saline solution given. Blood-pressure, 121 mm.

3.28.—100 c.c. saline solution given (grand total, 550 c.c.). Blood-pressure, 128 mm. A clot was removed from the carotid cannula.

3.31.—Blood-pressure, 110 mm. Respiratory failure occurred, and the pressure began to fall.

3.33.—Artificial respiration was begun.

3.34.—Blood-pressure, 78 mm. The artificial respiration was stopped. The respiration was slow and labored.

3.35.—Respiratory failure occurred, followed by cardiac failure. Recovery was brought about with artificial respiration. The dog was then killed.

Summary.—(1) Normal saline solution in excess of the amount of blood lost by 40 c.c. was infused at once after the hemorrhage stopped at the rate of 100 c.c. in two minutes, and brought the blood-pressure back to a point within one fifth of the original level; but the heart was overtaxed, the respiration temporarily embarrassed, and the blood-pressure began to fall steadily. (2) A total infusion of 240 c.c. above the amount of blood lost produced only a temporary rise in the blood-pressure, and death by respiratory failure followed in seven minutes.

EXPERIMENT 9

Hemorrhage; Normal Saline Infusion

SEPTEMBER, 1904.

Mongrel; weight, 5 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

9.00.—Control on drum. Blood-pressure, 170 mm.

9.07.—Control. Blood-pressure, 195 mm.

9.18.—Began to bleed. Artificial respiration was used momentarily. Blood-pressure, 189 mm.

9.26.—100 c.c. blood removed. Blood-pressure, 174 mm.

9.31.—Blood-pressure, 127 mm.

9.38.—100 c.c. blood removed. Artificial respiration was used momentarily. Blood-pressure, 82 mm. Compensation occurred before the control was taken.

9.41.—15 c.c. blood removed (total amount, 215 c.c.). Blood-pressure, 33 mm. There was sudden failure of respiration at the moment of taking the control, and gradual heart failure. The intravenous injection of normal saline solution was begun at once.

9.47.—75 c.c. saline solution given. The heart was massaged. There was partial recovery, but further attempts at recovery were ineffectual.

Note.—In this experiment the dog's respiration acted badly from the beginning. Using artificial respiration and stopping the ether gave marked relief, so that possibly the ether was an important factor in this experiment.

Summary.—In death from hemorrhage the respiratory center failed first.

EXPERIMENT 10

Hemorrhage; Normal Saline Infusion

SEPTEMBER, 1904.

Mongrel dog; weight, 15 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

9.26.—Control on drum. Blood-pressure, 170 mm. On burning a paw under light anesthesia there was a rise of pressure of 16 mm.

9.35.—Control. Blood-pressure, 161 mm. Began to bleed.

9.39½.—100 c.c. blood removed. Blood-pressure, 155 mm.

9.45.—100 c.c. blood removed. Blood-pressure, 135 mm.

9.50.—100 c.c. blood removed. Blood-pressure, 115 mm.

9.55.—100 c.c. blood removed. Blood-pressure, 75 mm.

10.02.—100 c.c. blood removed. Blood-pressure, 53 mm.

10.08.—100 c.c. blood removed. Blood-pressure, 36 mm.

10.13.—50 c.c. blood removed (total amount, 650 c.c.). Blood-pressure, 41 mm.

10.16.—Control. On burning a paw there was a rise of pressure of 5 mm.

10.20.—Control. Blood-pressure, 62 mm.

11.00.—Control. Blood-pressure, 59 mm.

11.13.—On burning a paw there was a rise of pressure of 13 mm.

11.15½.—Blood-pressure, 60 mm.

11.30.—Control. Blood-pressure, 69 mm.

11.35.—Began to inject normal saline solution intravenously. Blood-pressure, 69 mm.

11.37.—100 c.c. saline solution injected. Blood-pressure, 96 mm.

11.40.—100 c.c. saline solution injected. Blood-pressure, 109 mm.

11.45.—Blood-pressure, 100 mm.

11.50.—Began to inject the saline solution again very slowly.

12.00.—A clot was removed from the carotid cannula. Control. 50 c.c. saline solution injected. Blood-pressure, 109 mm.

12.12.—50 c.c. saline solution injected. The blood-pressure rose and fell—the presence of the clot explained part of the rise.

12.26.—Control. 50 c.c. saline solution injected. Blood-pressure, 106 mm., and falling with the dog partially coming out of the ether.

12.42.—50 c.c. saline solution injected. Blood-pressure, 99 mm.

1.01.—50 c.c. saline solution injected. Blood-pressure, 100 mm.

1.11.—50 c.c. saline solution injected. Blood-pressure, 114 mm.

1.20.—50 c.c. saline solution injected. Blood-pressure, 113 mm.

1.32.—50 c.c. saline solution injected (total amount, 550 c.c.). Blood-pressure, 111 mm. The respiration was scarcely embarrassed. The abdomen was slightly distended.

1.40.—Control.

1.42.—Control. Blood-pressure, 108 mm. On burning a paw there was a rise of pressure of 13 mm. The dog was killed by clamping the trachea.

Autopsy.—The right ventricle of the heart was apparently slightly dilated. There was slight edema of the pancreas and of the gut wall, but not of the stomach wall. There was no free fluid. The bladder was distended.

Summary.—(1) In a dog with high initial blood-pressure, poor reaction to peripheral stimulation three minutes after the removal of about three fifths the total amount of blood was associated with poor compensation after a wait of thirty-five minutes. Further stimulation excited the vasomotor center more, and the blood-pressure rose gradually for fifteen minutes. (2) The infusion of normal saline solution was begun eighty minutes after removing about three fifths the total amount of blood, and after full compensation had occurred. The first third of the solution, at the rate of 100 c.c. in three minutes, caused a rise of pressure which attained a level but little below the level reached by the infusion of the remaining two thirds. (3) After a rapid initial infusion of normal saline solution in amount equal to one third the amount of blood removed, the administration of the remaining two thirds, at a rate of 100 c.c. in twelve minutes, left the animal in good condition, with the vasomotor reflex active, although the blood-pressure was not brought back halfway to the initial height.

EXPERIMENT 11

Dogs A and B.—Hemorrhage; Normal Saline Infusion

SEPTEMBER, 1904.

Dog A.—Weight, 11.8 kilos; condition, good. Dog B.—Weight, 12.7 kilos; condition, good. At first chloroform and then ether anesthesia were given through a tracheal cannula. Other arrangements were as in Experiment 1, except that both dogs recorded on the same drum.

2.20.—Control on drum. Dog A.—Blood-pressure, 124 mm. Dog B.—Blood-pressure, 150 mm.

2.40.—Began to bleed. Dog A.—Blood-pressure, 109 mm. Dog B.—Blood-pressure, 137 mm.

2.54.—Dog A.—200 c.c. blood removed. Blood-pressure, 59 mm. Dog B.—100 c.c. blood removed. Blood-pressure, 94 mm. Up to this time chloroform was used for the anesthetic, and then ether was substituted for it. Dog B compensated entirely for the amount of blood lost during this interval.

3.00.—Dog A.—Blood-pressure, 48 mm. Dog B.—Blood-pressure, 143 mm.

3.09.—Dog A.—100 c.c. blood removed. Blood-pressure, 44 mm. Dog B.—200 c.c. blood removed. Blood-pressure, 116 mm.

3.17.—Dog A.—100 c.c. blood removed (total amount, 400 c.c.). Blood-pressure, 39 mm. Dog B.—100 c.c. blood removed. Blood-pressure, 80 mm.

3.22.—Dog A.—Blood-pressure, 36 mm. Dog B.—100 c.c. blood removed. Blood-pressure, 44 mm.

3.26.—Dog A.—Blood-pressure, 41 mm. Dog B.—100 c.c. blood removed (total amount, 600 c.c.). Blood-pressure, 37 mm.

3.30.—Dog A.—Blood-pressure, 41 mm. Dog B.—Blood-pressure, 45 mm.

3.45.—Dog A.—Blood-pressure, 25 mm. Artificial respiration was begun. Dog B.—Blood-pressure, 82 mm.

3.51.—Dog A.—Cardiac and respiratory failure occurred. The intravenous injection of normal saline solution was begun, and 100 c.c. were injected rapidly. Dog B.—Blood-pressure, 80 mm.

3.55.—Dog A.—Massage of the heart was ineffectual and the dog died.

4.00.—Dog B.—Blood-pressure, 92 mm. (From this point the data refer to Dog B.)

4.15.—Blood-pressure, 90 mm.

4.30.—Blood-pressure, 76 mm.

4.38.—Blood-pressure, 64 mm.

4.40.—Blood-pressure, 68 mm. Began to inject saline solution intravenously.

4.43.—Blood-pressure, 81 mm. 50 c.c. saline solution injected.

4.47.—Blood-pressure, 98 mm. 50 c.c. saline solution injected.

4.50.—Blood-pressure, 102 mm. 50 c.c. saline solution injected.

4.59.—Blood-pressure, 109 mm. 100 c.c. saline solution injected.

5.02½.—Blood-pressure, 110 mm. 50 c.c. saline solution injected.

5.06.—Blood-pressure, 108 mm. 50 c.c. saline solution injected.

5.09.—Blood-pressure, 112 mm. 50 c.c. saline solution injected.

5.10.—Began to give the saline solution rapidly.

5.10½.—50 c.c. saline solution injected. Blood-pressure, 114 mm.

5.11¼.—50 c.c. saline solution given (total amount, 500 c.c.). Blood-pressure, 112 mm.

5.18.—Blood-pressure, 107 mm. The experiment was stopped on account of darkness.

Summary.—Dog A.—In a dog with respiratory and cardiac failure occurring twenty-four minutes after a hemorrhage of about two fifths of the total amount of blood with poor compensation, the intravenous injection of normal saline solution was ineffectual. Dog B.—(1) After a hemorrhage of about three fifths of the total amount of blood, spontaneous compensation brought the blood-pressure back to over one half the original level, and maintained it there for seventy-five minutes. (2) At the end of this time the intravenous injection of normal saline solution was given while marked compensatory power was still being shown, and the blood-pressure was still further raised to three fifths of the original level.

EXPERIMENT 12

Hemorrhage; Normal Saline Infusion; Adrenalin

SEPTEMBER, 1904.

Mongrel dog; weight, 10 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

9.46.—Control on drum. Blood-pressure, 161 mm.

9.55.—Blood-pressure, 154 mm. On burning a paw there was a rise of pressure of 16 mm. The femoral cannula was put in place.

10.01.—Control. Blood-pressure, 146 mm. Began to bleed.

10.06.—100 c.c. blood removed. Blood-pressure, 105 mm.

10.13.—100 c.c. blood removed. Blood-pressure, 82 mm.

10.21.—100 c.c. blood removed. Blood-pressure, 46 mm.

10.32.—100 c.c. blood removed (total amount, 400 c.c.). Blood-pressure, 38 mm.

10.45.—Control. Blood-pressure, 56 mm.

10.53.—Control. Blood-pressure, 120 mm.

10.55.—Control. Blood-pressure, 108 mm.

11.00.—Control. Blood-pressure, 82 mm.

11.13.—Control. Blood-pressure, 35 mm. Respiratory failure occurred, and rapid cardiac failure. Artificial respiration was begun.

11.15½.—Began to inject rapidly normal saline solution intravenously. 250 c.c. were given, and first 2, and then 3, and finally 16 minims of 1–1,000 adrenalin chlorid solution, but these measures and massage of the heart were ineffectual, and the dog died.

Summary.—(1) In a dog with active vasomotor centers, compensation at the end of the hemorrhage was immediate, and extremely marked. (2) Marked compensation after hemorrhage was rapidly followed by respiratory and cardiac failure, perhaps because the circulation was not supported with saline infusion soon enough after the compensation occurred.

EXPERIMENT 13

Hemorrhage; Normal Saline Infusion; Strychnin; Adrenalin

September 18, 1904.

Mongrel dog; weight, 12.5 kilos; condition, good. The thyroid gland was enlarged. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

1.45.—Control on drum. Cannulæ were placed in the femoral artery and vein. Blood-pressure, 162 mm.

1.52.—Control. Blood-pressure, 152 mm. On burning a paw there was an initial fall of pressure of 10 mm. followed by recovery to 152 mm.

1.54½.—Began to bleed.

1.58½.—100 c.c. blood removed. Blood-pressure, 144 mm.

2.04.—100 c.c. blood removed. Blood-pressure, 130 mm.

2.09.—100 c.c. blood removed. Blood-pressure, 122 mm.

2.14.—100 c.c. blood removed. Blood-pressure, 82 mm.

2.19.—100 c.c. blood removed. Blood-pressure, 48 mm.

2.25.—100 c.c. blood removed (total amount, 600 c.c.). Blood-pressure, 41 mm.

2.30.—On burning a paw there was a slight initial drop in the pressure followed by a rise of 9 mm.

2.55.—Control. Blood-pressure, 58 mm.

3.10.—Control. Blood-pressure, 54 mm.

3.25.—Control. Blood-pressure, 51 mm.

3.34½.—Control. On burning a paw there was no effect.

3.35.—Began to inject normal saline solution intravenously. Blood-pressure, 36 mm.

3.37.—100 c.c. saline solution injected. Blood-pressure, 36 mm.

3.39.—Control.

3.40.—Began saline infusion again.

3.43.—100 c.c. saline solution injected. Blood-pressure, 40 mm. Artificial respiration was used. The abdomen was distended.

3.46.—100 c.c. saline solution injected. Blood-pressure, 40 mm.

3.47.—100 c.c. saline solution injected. Blood-pressure, 42 mm. The artificial respiration was stopped.

3.48.—The saline infusion was resumed.

3.51.—100 c.c. saline solution injected. Blood-pressure, 45 mm.

3.55.—100 c.c. saline solution injected (total amount, 600 c.c.). Blood-pressure, 55 mm.

4.00.—Blood-pressure, 48 mm. On burning a paw there was no reaction.

4.03.—Blood-pressure, 46 mm. $\frac{1}{150}$ grain strychnin (0.034 mgm. per kilo) was given in 100 c.c. saline solution, and repeated twice with one-minute interval between.

4.08.—Blood-pressure, 46 mm. Two more doses of the same amount of strychnin were given. This made a total of 0.17 mgm. per kilo, or a one half tetanic dose. The blood-pressure was not affected.

4.11.—Blood-pressure, 46 mm.

4.12.—Blood-pressure, 42 mm.

4.13½.—Artificial respiration was begun. Pressure on the abdomen caused a temporary rise of blood-pressure. Blood-pressure, 36 mm. The dog was in a general tonic condition. There were no convulsions.

4.16.—10 minims of 1–1,000 adrenalin solution were given intravenously. The splanchnic area was engorged with fluid. Blood-pressure, 66 mm.

4.18.—Blood-pressure, 60 mm. The breathing was spontaneous. There were slight strychnin convulsions.

4.24½.—Blood-pressure, 47 mm. Partial bandaging of the extremities was begun. The blood-pressure rose 9 mm.

4.29.—20 minims of adrenalin solution were given. Blood-pressure, 106 mm. The pressure gradually fell to the abscissa in two minutes.

Summary.—(1) After a hemorrhage of about three fifths the total amount of blood, feeble reaction to peripheral stimulation was associated with poor compensation. (2) Spontaneous failure of compensation was associated with failure to react to peripheral stimulation. (3) The infusion of normal saline solution, in amount equal to the amount of blood removed, was begun sixty-five minutes after the blood was removed. It did not raise the blood-pressure over 20 mm., embarrassed the respiration before it was half given, and caused overtaxing of the heart, which was gradually followed by more normal action. (4) Peripheral stimulation after hemorrhage, failure of compensation, a wait of an hour, and then saline infusion evoked no response. (5) After the above procedures adrenalin caused a considerable temporary rise of blood-pressure, which was followed by rapid cardiac failure.

EXPERIMENT 14

Hemorrhage; Adrenalin; Normal Saline Infusion

SEPTEMBER 4, 1904.

Bull terrier bitch; weight, 10.9 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

11.18.—Control on drum. Blood-pressure, 154 mm.

11.21.—Began to bleed.

11.25.—100 c.c. blood removed.

11.30.—100 c.c. blood removed.

11.35.—100 c.c. blood removed.

11.39.—100 c.c. blood removed. Blood-pressure, 63 mm.

11.53.—Blood-pressure, 95 mm.

11.54.—Began to bleed again.

11.57.—100 c.c. blood removed.

12.03.—Control. 85 c.c. blood removed. Blood-pressure, 50 mm. On burning a paw a rise of 12 mm. was followed by a temporary fall, and then a rise to a higher level of 65 mm.

12.20.—The sciatic nerve was exposed. Blood-pressure, 62 mm. The sciatic nerve was stimulated. Interference with the respiration occurred.

12.29.—Stopped the drum. Blood-pressure, 69 mm.

12.30.—Blood-pressure, 68 mm.

12.36.—Blood-pressure, 72 mm. Began to bleed.

12.39.—Total amount of blood removed, 615 c.c.

12.42.—Control. Blood-pressure, 51 mm. On stimulating the sciatic nerve a rise of 7 mm. occurred, and was maintained for five minutes.

12.50.—Blood-pressure, 48 mm.

12.52.—On burning a paw there was a rise of blood-pressure of 2 mm.

12.53½.—On stimulating the sciatic nerve there was no effect.

12.58.—Blood-pressure, 42 mm. The heart action began to be very irregular, and the respiration began to fail.

1.00½.—On burning a paw there was no effect.

1.01.—Artificial respiration was begun. Blood-pressure, 32 mm. Normal saline solution and adrenalin were started intravenously, but there was no effect except a slight momentary improvement of the pulse wave.

Summary.—(1) Peripheral stimulation after hemorrhage (after compensation had been overcome by further bleeding) produced a very slight effect, but the blood-pressure remained higher afterwards. (2) The same was true of sciatic stimulation twenty minutes after stopping the bleeding. (3) After a certain length of time reaction to peripheral and sciatic stimulation disappeared entirely, and was associated with falling of the blood-pressure to death. (4) After a certain time following hemorrhage the intravenous injection of normal saline solution and adrenalin chlorid had no effect—in this case one hour after about seven tenths the total amount of blood was removed, although there was still sufficient circulation to distribute the fluid.

EXPERIMENT 15

Hemorrhage; Adrenalin; Normal Saline Infusion; Digitalin

SEPTEMBER 13, 1904.

Fox terrier dog; weight, 7.7 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.50.—Blood-pressure, 174 mm. Femoral cannula put in place.

11.00.—Blood-pressure, 150 mm. Began to bleed.

11.05.—100 c.c. blood removed. Blood-pressure, 78 mm.

11.09.—100 c.c. blood removed. Blood-pressure, 42 mm.

11.12.—45 c.c. blood removed. Blood-pressure, 34 mm.

11.12½.—On burning a paw there was a rise in pressure of 8 mm.

11.12¾.—On stimulating the sciatic nerve there was a very slight

fall of blood-pressure, followed by recovery to the former level. The larynx was opened.

11.14.—On manipulating the larynx there was no effect on the blood-pressure, but there was slight respiratory inhibition.

11.15$\frac{1}{4}$.—On burning a paw there was a slight rise in pressure.

11.18.—Blood-pressure, 81 mm. Began to bleed again.

11.20.—60 c.c. blood removed (total amount, 305 c.c.). Blood-pressure, 26 mm. Cardiac and respiratory failure occurred. Artificial respiration was given. The intravenous injection of normal saline solution was begun. 4 minims of 1–1,000 adrenalin chlorid solution were injected.

11.25.—125 c.c. saline solution injected.

11.26.—Blood-pressure, 42 mm. The dog recovered.

11.27.—Blood-pressure, 54 mm.

11.30.—75 c.c. saline solution injected. Blood-pressure, 81 mm.

11.32.—100 c.c. saline solution injected (total amount, 300 c.c.). Blood-pressure, 103 mm.

11.36.—Blood-pressure, 95 mm.

11.36$\frac{1}{2}$.—On burning a paw there was a rise of pressure of 12 mm.

11.40.—Blood-pressure, 90 mm. On stimulating the sciatic nerve there was a slight fall of pressure, followed by slow recovery.

11.43.—Blood-pressure, 74 mm.

11.44.—$\frac{1}{100}$ grain digitalin (0.65 kgm. per kilo) was given intravenously in 10 c.c. normal saline solution.

11.45.—Blood-pressure, 74 mm.

11.46.—Blood-pressure, 76 mm. The pulse wave was not affected.

11.50.—Cardiac failure occurred. The use of artificial respiration, saline infusion, adrenalin, and massage was ineffectual.

Summary.—(1) After a fall in the blood-pressure from hemorrhage the vascular reflexes were depressed; they were then stimulated by the addition of saline solution to the blood stream. (2) Adrenalin and normal saline solution given intravenously were effectual in overcoming cardiac failure nine minutes after the greater part of the hemorrhage had occurred. (3) Rapidly given normal saline solution (100 c.c. per minute) in amount equal to the amount of blood lost, with 4 minims of 1–1,000 adrenalin chlorid solution, brought the blood-pressure up to one half its initial level with marked increase in the size of the pulse wave, but in five minutes this was followed by diminution in size of the wave and fall of pressure, and death occurred in twenty-seven minutes from acute dilatation of the heart.

EXPERIMENT 16

Hemorrhage; Normal Saline Infusion; Atropin; Adrenalin

September, 1904.

Yellow mongrel dog; weight, 14 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.40.—Control on drum. Blood-pressure, 172 mm. The femoral cannula was put in place.

10.47.—Blood-pressure, 160 mm.

10.48.—Began to bleed.

10.56½.—Blood-pressure, 112 mm.

11.13.—500 c.c. blood removed. Blood-pressure, 54 mm.

11.17.—100 c.c. blood removed. There was compensation of the pressure to 60 mm., and then a fall.

11.22.—Blood-pressure, 62 mm. On burning a paw there was a rise of pressure of 22 mm., which was maintained.

11.25.—Blood-pressure, 78 mm.

11.33.—Control. Blood-pressure, 78 mm. On burning a paw there was a rise of 29 mm.

11.34½.—Blood-pressure, 103 mm.

11.44.—Control. Blood-pressure, 86 mm. On burning a paw there was a rise of 24 mm.

11.47.—Control. Blood-pressure, 96 mm. Began to bleed.

11.54.—150 c.c. blood removed.

11.59.—Control. Blood-pressure, 60 mm.

12.02.—100 c.c. blood removed (total amount, 850 c.c.). Blood-pressure, 37 mm. On burning a paw there was a steady rise of 5 mm. On stimulating the sciatic nerve there was a slight fall with recovery to the first level.

12.04½.—After laryngeal manipulation there was slight respiratory inhibition, and no effect on the blood-pressure.

12.05.—Stopped the drum. Blood-pressure, 42 mm.

12.06½.—Began to inject normal saline solution intravenously. Blood-pressure, 42 mm.

12.09½.—100 c.c. saline solution injected. Blood-pressure, 59 mm.

12.12½.—Control. 100 c.c. saline solution injected. Blood-pressure, 67 mm.

12.15.—Control. 100 c.c. saline solution injected. Blood-pressure, 90 mm.

12.18.—Control. 100 c.c. saline solution injected. Blood-pres-

sure, 85 mm.—the fall was due to ether. The respiration was slightly stronger.

12.21.—Control. Blood-pressure, 105 mm. 100 c.c. saline solution injected.

12.23.—Control. Blood-pressure, 100 mm. 100 c.c. saline solution injected.

12.26.—Control. Blood-pressure, 104 mm. 100 c.c. saline solution injected (total amount, 700 c.c.).

12.26½.—On burning a paw there was a rise of pressure of 8 mm.

12.27½.—On stimulating the sciatic nerve there was a fall of pressure of 20 mm., followed by a rise of 10 mm.

12.28.—After manipulating the larynx there was a slight slowing of respiration and some fall in pressure.

12.29.—Blood-pressure, 90 mm. $\frac{1}{50}$ grain of atropin (0.09 mgm. per kilo) was given in 5 c.c. saline solution intravenously.

12.31½.—Blood-pressure, 58 mm. 1 c.c. 1–1,000 adrenalin chlorid solution was given in 40 c.c. saline solution. There was a rise of the pressure to 90 mm., with an immediate fall.

12.33.—Blood-pressure, 56 mm.

12.34½.—Blood-pressure, 54 mm.

12.35.—Control. On burning a paw there was a steady rise of pressure of 6 mm.

12.37.—Control. On stimulating the sciatic nerve there was a temporary fall of pressure of 4 mm., succeeded by a steady rise.

12.38.—Manipulating the larynx had no effect except to slow the respiration. Blood-pressure, 65 mm.

12.40.—$\frac{1}{150}$ grain atropin (0.03 mgm. per kilo) was given in 5 c.c. saline solution.

12.41.—Slow, continuous saline infusion was started, giving it for two and one half minutes at a time at one and one half minute intervals. Each administration of four doses was followed by a rise of about 30 mm. of pressure, with an immediate fall to the former level.

Summary.—(1) In a dog showing good compensation after a hemorrhage of about one half the total amount of blood, reaction to peripheral stimulation was very marked up to the height of compensation, which occurred in twenty minutes. (2) On bleeding further until there was no compensation, the reaction to peripheral stimulation was almost entirely lost. (3) Normal saline solution injected intravenously in amount equal to the amount of blood lost, beginning fifty minutes after the bulk of the bleeding and given at the rate of 100 c.c. in three minutes, brought back the blood-pressure to one

half the initial level, where it was sustained for eight minutes, until further procedures were instituted. (4) All stimulation of the reflexes produced much more effect after the saline solution was given. (5) When atropin was given after hemorrhage and saline solution it caused a marked fall of blood-pressure. (6) Injection of adrenalin was followed by a rise and then a fall to a lower level after hemorrhage and saline infusion. (7) After hemorrhage and saline infusion (100 c.c. in three minutes), with the use of atropin and adrenalin also, reaction to peripheral stimulation, which had increased after the saline infusion, diminished again in nine minutes.

EXPERIMENT 17

Hemorrhage; Strychnin

AUGUST 11, 1904.

Fox terrier dog; weight, 9.5 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

11.00.—Control on drum. Blood-pressure, 142 mm. Bled 100 c.c. slowly from femoral artery.

11.15.—Blood-pressure, 94 mm. $\frac{1}{10}$ grain strychnin (0.68 mgm. per kgm. of body weight) injected into the external jugular vein produced convulsions, with an accompanying rise of blood-pressure. With the stopping of the convulsions the blood-pressure rose to the height of the original control. The respiration was slowed and the pulse waves were higher.

11.30.—Bled 100 c.c. (total amount, 200 c.c.). Blood-pressure fell to 66 mm. Gave another injection of $\frac{1}{10}$ grain strychnin (0.68 mgm. per kilo) as before, and the blood-pressure fell gradually to 14 mm., with very slight convulsions occurring. The heart rate diminished and the height of the pulse wave increased with cardiac and then respiratory failure in a few minutes. Artificial respiration brought return of function. The animal continually showed strychnin tremors. Blood-pressure, 70 mm.

11.55.—Death from respiratory failure.

Summary.—A large overdose of strychnin in a moderate hemorrhage (about one seventh the total amount of blood) affected the heart relatively more than the blood-pressure. In a hemorrhage of about one third the total amount of blood a repetition of the same dose produced an immediate cardiac failure. The strychnin convulsions were diminished by bleeding.

EXPERIMENT 18

Hemorrhage; Strychnin

August 12, 1904.

Skye terrier dog; weight, 7.7 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

11.10.—Control on drum. Blood-pressure, 146 mm. Bled 100 c.c. (about one sixth the total amount of blood). The blood-pressure fell to 86 mm.

11.28.—The blood-pressure rose to 110 mm. A tetanic dose of strychnin, $\frac{1}{20}$ grain (0.4 + mgm. per kilo), injected into the external jugular vein produced extreme convulsions, which occurred at intervals of about three minutes and lasted throughout the experiment. The convulsions reached their maximum two minutes after the administration of the strychnin. The blood-pressure at its greatest height was 168 mm. The respiration was very materially affected. Periodic failures were overcome by artificial respiration. When the convulsions became less frequent the blood-pressure level was considerably below that following the hemorrhage, and showed a general falling tendency which at no time reached the hemorrhage level.

12.05.—Death occurred from respiratory failure.

Summary.—After a moderate hemorrhage (about one sixth the total amount of blood) a tetanic dose of strychnin raised the blood-pressure 22 mm. above the original level.

EXPERIMENT 19

Hemorrhage; Strychnin

August 13, 1904.

Fox terrier dog; weight, 9 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

9.46.—Control on drum. Blood-pressure, 142 mm.

9.50.—Control. Blood-pressure, 110 mm. The fall in blood-pressure was due to an accidental hemorrhage of about 40 c.c. which occurred while inserting the cannula in the femoral artery. This was followed by an immediate compensatory rise to 126 mm.

9.55.—Began bleeding rather rapidly.

9.56.—265 c.c. of blood removed (total amount, about 305 c.c.). The blood-pressure fell to 28 mm., but at once began to rise. The anesthetic was removed. The respiration was good.

10.02.—Blood-pressure, 66 mm. $\frac{1}{20}$ grain strychnin (0.36 mgm. per kilo) was injected into the external jugular vein. It took effect in one minute and the blood-pressure rose to 140 mm. Slight convulsions were produced.

10.10.—Control. The effects of the strychnin were still shown. The blood-pressure ranged from 108 to 154 mm. until 10.18. The respirations were shallow. Artificial respiration was used.

10.18 to 10.27.—In this time three convulsions occurred, with the blood-pressure steadily tending to fall.

10.28.—Blood-pressure, 22 mm. Cardiac and respiratory failure occurred. Artificial respiration was used.

10.48.—Control. Blood-pressure, 24 mm.

10.55.—Control. Blood-pressure, 16 mm. The dose of $\frac{1}{20}$ grain (0.36 mgm. per kilo) was repeated as before. Tremors of the neck muscles occurred. Artificial respiration was used. There was gradual failure of the heart.

Summary.—(1) With the dog in good condition, compensation following a very rapid hemorrhage of about five thirteenths the total amount of blood was immediate and marked. (2) A seven eighths tetanic dose of strychnin brought on convulsions after a considerable latent period. The blood-pressure was raised barely to the original level at once, and then immediately fell, signs of cardiac failure being apparent in fifteen minutes. (3) On repeating the dose of strychnin with the animal moribund no effect was produced.

EXPERIMENT 20

Hemorrhage; Strychnin

AUGUST 15, 1904.

Fox terrier; weight, 9.5 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

2.54.—Control on drum. Blood-pressure, 162 mm.

3.04.—Control. Blood-pressure, 146 mm. Femoral cannula put in place.

3.08½.—Control. Began to bleed. The blood-pressure fell to 28 mm. Bled 225 c.c. The blood-pressure began slowly to rise, but was maintained at 32 mm. by slowly bleeding 40 c.c. more (total amount, 265 c.c.).

3.18½.—Blood-pressure, 32 mm. A dose of $\frac{1}{20}$ grain strychnin (0.34 + mgm. per kilo) given intravenously produced effect in half a minute, throwing the animal into rapid, short, successive convul-

sions. The blood-pressure at the initial convulsion rose to 62 mm., and then maintained a level of about 50 mm., with a slightly rising tendency. Artificial respiration was continued throughout until the drum was stopped at 3.23½. Stoppage of the artificial respiration produced death from asphyxia.

Summary.—(1) After a very rapid hemorrhage the blood-pressure continued to fall four minutes before compensation began. (2) What was calculated to be a slightly less than tetanic dose of strychnin was given just after the loss of about two fifths the total amount of blood. The low level of the blood-pressure was maintained by further slow bleeding for ten minutes. The strychnin caused convulsions after a latent period of half a minute, but the blood-pressure level was raised only 30 mm., although the length of the pulse wave was increased.

EXPERIMENT 21

Dog A.—Hemorrhage; Strychnin. Dog B.—Shock; Strychnin

September, 1904.

Dog A.—Weight, 7.2 kilos; condition, good. Dog B.—Weight, 13.2 kilos; condition, good. Ether anesthesia for each dog through tracheal cannula. Other arrangements as in Experiment 1, with both dogs recording on the same drum.

9.35.—Control on drum. Dog A.—Blood-pressure, 148 mm. Dog B.—Blood-pressure, 156 mm.

9.45.—A paw of each dog was burned. Dog A.—There was a rise of pressure of 9 mm. Dog B.—There was a rise of pressure of 15 mm.

9.50.—Dog A.—Blood-pressure, 132 mm. Dog B.—Blood-pressure, 140 mm. On stimulating a sciatic nerve of each dog there was a rise of pressure in Dog A of 8 mm., and in Dog B an initial fall of pressure and then a rise of 9 mm.

10.00.—Control. Dog B.—A clot was removed from the carotid cannula. Dog A.—Blood-pressure, 136 mm.

10.03.—Control. Dog A.—Blood-pressure, 135 mm. Dog B.—Blood-pressure, 130 mm.

10.04.—Dog A.—Began to bleed.

10.23.—Dog A.—300 c.c. blood removed. Blood-pressure, 85 mm. Dog B.—Blood-pressure, 136 mm.

10.28.—Control. Dog A.—50 c.c. blood removed (total amount, 350 c.c.). Blood-pressure, 63 mm. Dog B.—Blood-pressure, 138 mm.

11.15.—Dog A.—Blood-pressure, 52 mm. Dog B.—Caused shock. Blood-pressure, 92 mm.

11.17.—On burning a paw of each, Dog A showed a rise of pressure of 19 mm., and Dog B of 25 mm.

11.25.—Dog A.—Blood-pressure, 62 mm. Dog B.—Blood-pressure, 104 mm. On stimulating a sciatic nerve of each dog, Dog A showed a rising and falling pressure, and Dog B (more ether was given just then) showed an initial fall and a rise of 8 mm., with a sudden second fall and a rise of 6 mm.

11.32.—Both dogs were deeply anesthetized. Dog A.—Artificial respiration was begun. Blood-pressure, 55 mm. Dog B.—On stimulating the sciatic nerve there was a fall of pressure, with slow recovery to the former level. Blood-pressure, 101 mm.

11.41.—Dog A.—The artificial respiration was stopped. The sciatic nerve of both dogs was stimulated. Dog A.—Blood-pressure, 51 mm. The stimulation produced no effect. Dog B.—Blood-pressure, 106 mm. The effect of the stimulation was the same as at the previous time.

11.50.—Dog A.—Blood-pressure, 49 mm. $\frac{1}{150}$ grain strychnin (.059 mgm. per kilo) was injected intravenously. Dog B.—Blood-pressure, 109 mm. The same amount of strychnin was given (for this dog .032 mgm. per kilo).

11.55.—Dog A.—There was a steady fall in pressure to 17 mm., and then cardiac failure occurred. Dog B.—Blood-pressure, 108 mm. The strychnin produced no effect. On stimulating the sciatic nerve there was a fall of pressure with slow recovery to normal.

12.01.—Dog B.—Blood-pressure, 105 mm. $\frac{1}{75}$ grain of strychnin (.065 mgm. per kilo) was given.

12.06.—Dog B.—Blood-pressure, 108 mm. The dog was then killed.

EXPERIMENT 22

Hemorrhage; Normal Saline Infusion; Strychnin

September 21, 1904.

Mongrel dog; weight, 9.5 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

9.01.—Control on drum. Blood-pressure, 146 mm.

9.21.—Control. Blood-pressure, 136 mm.

9.22.—On burning a paw there was a rise in pressure of 36 mm.

9.23.—Began to bleed.

9.28.—100 c.c. blood removed. Blood-pressure, 131 mm.

9.34.—100 c.c. blood removed. Blood-pressure, 108 mm.

9.39.—100 c.c. blood removed. Blood-pressure, 61 mm.

9.43.—100 c.c. blood removed. Blood-pressure, 54 mm.

9.46.—50 c.c. blood removed (total amount, 450 c.c.). Blood-pressure, 44 mm.

9.49.—Control. Blood-pressure, 82 mm.

9.54.—The ether was stopped. Blood-pressure, 68 mm.

10.00.—Ether resumed. Blood-pressure, 58 mm.

10.05.—Control. Blood-pressure, 72 mm.

10.08.—Respiratory failure occurred. Blood-pressure, 40 mm. Artificial respiration brought about recovery.

10.12½.—Began to inject normal saline solution intravenously. Blood-pressure, 42 mm.

10.13.—50 c.c. saline solution were given in half a minute. Blood-pressure, 48 mm.

10.18.—100 c.c. saline solution were given in five minutes. Blood-pressure, 77 mm.

10.27.—150 c.c. saline solution were given in nine minutes. Blood-pressure, 46 mm.

10.35.—Respiratory failure occurred, and the dog was pulseless. Blood-pressure, 23 to 42 mm.

10.36.—50 c.c. more saline solution were rapidly given (total amount up to this point, 350 c.c.), and $\frac{1}{150}$ grain strychnin (0.04 mgm. per kilo).

10.39.—Control. Blood-pressure, 38 mm. There were slight muscular tremors.

10.42.—Began to inject saline solution again. Blood-pressure, 46 mm.

10.47.—Control. Blood-pressure, 48 mm. The respiration was failing and artificial respiration was begun.

10.49.—Control. Blood-pressure, 52 mm. Artificial respiration was stopped. 50 c.c. saline solution were given.

10.52½.—Control. Blood-pressure, 56 mm. 50 c.c. saline solution were given (grand total, 450 c.c.). There were tremors which were apparently due to the strychnin.

10.59.—The respiration was failing. Blood-pressure, 48 mm. Artificial respiration was started. Cardiac failure occurred. The heart was massaged.

11.01.—The artificial respiration was stopped. Recovery followed. Blood-pressure, 51 mm.

11.09.—Blood-pressure, 48 mm.

11.12.—Blood-pressure, 36 mm. The dog was again rapidly failing, and was killed.

Summary.—(1) In a dog with active vasomotor centers, compensation at the end of the hemorrhage was immediate and extremely marked. (2) The marked compensation after hemorrhage when not supported by saline infusion was rapidly followed by respiratory and cardiac failure. (3) After cardiac and respiratory failure the intravenous injection of normal saline solution brought about recovery at first rapidly, and then very slowly, but did not raise the blood-pressure except very temporarily, and this was followed in a few minutes by a similar failure. The effect of further saline infusion was only to cause an overtaxation of the heart which resulted in acute dilatation. (4) A therapeutic dose of strychnin after cardiac and respiratory failure subsequent to compensation had no effect in assisting normal saline infusion to bring about a return of the normal functions.

EXPERIMENT 23

Hemorrhage; Normal Saline Infusion; Strychnin

SEPTEMBER 16, 1904.

Mongrel; weight, about 10 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.05.—Control on drum. Blood-pressure, 165 mm. Began to bleed rapidly.

10.15.—450 c.c. blood removed. Began to inject normal saline solution intravenously.

100 c.c. saline solution injected. Blood-pressure, 65 mm.
100 c.c. saline solution injected. Blood-pressure, 108 mm.
100 c.c. saline solution injected. Blood-pressure, 126 mm.
100 c.c. saline solution injected. Blood-pressure, 142 mm.
100 c.c. saline solution injected (total amount, 500 c.c.). Blood-pressure, 146 mm.

10.40.—Control. Blood-pressure, 135 mm. $\frac{1}{5}$ grain strychnin (1.2 mgm. per kilo) was given intravenously. An intense convulsion occurred which was followed by death.

Summary.—(1) The infusion of normal saline solution (50 c.c. more than the amount of blood removed) was given at a rate of 100 c.c. in two minutes, beginning seven minutes after the hemorrhage ceased, and in two minutes brought the blood-pressure back to the original level, but the respirations were labored and the heart

was overtaxed. (2) A large overdose of strychnin after hemorrhage and recovery by saline infusion produced the characteristic rise of blood-pressure with convulsions.

EXPERIMENT 24

Hemorrhage; Normal Saline Infusion; Strychnin

SEPTEMBER 7, 1904.

Mongrel fox terrier; weight, 10.5 kilos; condition, good. The thyroid gland was enlarged. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

11.15.—Control on drum. Blood-pressure, 168 mm.

11.29.—Control. A clot in the carotid cannula was removed. Blood-pressure, 165 mm.

11.30.—Began to bleed.

11.44.—300 c.c. blood removed. Blood-pressure, 38 mm.

11.45.—On burning a paw there was a rise in pressure of 2 mm. The sciatic nerve was exposed.

11.49.—Control. Blood-pressure, 35 mm. After stimulating the sciatic nerve there was a slight fall of pressure with recovery.

11.52.—Blood-pressure, 37 mm. After laryngeal manipulation there was a very slight fall of pressure with recovery.

11.54.—Blood-pressure, 40 mm. Began to inject normal saline solution intravenously.

11.58.—200 c.c. saline injected. Blood-pressure, 75 mm. There was a marked improvement of cardiac and respiratory tone.

11.59½.—Continued the saline solution injection.

12.03.—Saline injection stopped.

12.04.—Control. Blood-pressure, 106 mm. Saline injection started. Artificial respiration begun. There was a fall in the blood-pressure, followed by a rise.

12.10.—Blood-pressure, 98 mm. Maximum systolic pressure, 106 mm. Minimum diastolic pressure, about 84 mm. 100 c.c. saline solution injected (total amount, 300 c.c.).

12.10½.—On burning a paw there was a rise of blood-pressure of 12 mm., which was maintained.

12.11½.—Stimulating the sciatic nerve had no appreciable effect except to lower the minimum diastolic pressure.

12.18.—Blood-pressure, 70 mm.

12.19½.—On burning a paw there was a rise of pressure of 18 mm., with a variable pressure level following.

12.21.—After manipulating the larynx there was a temporary cardiac inhibition with recovery.

12.32.—$\frac{1}{150}$ grain strychnin (0.04 mgm. per kilo) was given intravenously with 10 c.c. normal saline solution. Blood-pressure, 71 mm.

12.36.—The dose of strychnin was repeated. Blood-pressure, 80 mm.

12.40.—Blood-pressure, 81 mm. $\frac{1}{150}$ grain strychnin (0.04 mgm. per kilo) was injected into the external jugular vein. This gave a total dose of strychnin of 0.12 mgm. per kilo, i. e., a one half tetanic dose. No convulsions occurred.

12.44.—The blood-pressure rose to 196 mm.

12.48.—Blood-pressure, 92 mm. The blood-pressure then fell until death occurred.

Summary.—(1) Fourteen minutes after stopping the hemorrhage the infusion of normal saline solution in amount equal to the quantity of blood lost, and at the rate of 100 c.c. in two minutes, was followed by considerable reaction on giving the dog peripheral and sciatic stimulation. (2) This amount of saline infusion given at this rate (100 c.c. in two minutes) brought back the blood-pressure to five thirteenths of the original level, and in eighteen minutes it was back within 18 mm. of the original level. (3) The height of the pulse wave was increased almost one third at the end of this rapid infusion. (4) Strychnin in one half tetanic dose after hemorrhage, partially compensated with saline solution, produced no convulsions, but caused a rise of blood-pressure higher than the original level, which was quickly followed by cardiac failure.

EXPERIMENT 25

Hemorrhage; Strychnin; Normal Saline Infusion

August 17, 1904.

Fox terrier dog; weight, 10 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

11.40.—Control on drum. Blood-pressure, 174 mm.

11.48.—Began to bleed at a regular rate with the blood rapidly dropping out of the cannula in the femoral artery. The blood-pressure did not fall uniformly, as it was sustained at the same level for a while in the middle of the bleeding. The initial fall was much more rapid than the fall after this period. The pressure fell to 110 mm.

11.50.—Blood-pressure, 86 mm. 300 c.c. blood removed.

11.57.—Blood-pressure, 96 mm.—slight compensation.

11.58.—Bled 50 c.c. more (total amount, 350 c.c.). Blood-pressure, 34 mm.

12.07.—Control. Blood-pressure, 46 mm. The breathing was spasmodic.

12.10.—On burning a paw the reflex action was delayed. There was no corneal reflex.

12.12½.—Injected $\frac{1}{150}$ grain strychnin (0.04 mgm. per kilo) into the external jugular vein. Blood-pressure, 54 mm.

12.17.—Blood-pressure still 54 mm., so that it was not affected in four and a half minutes. The respirations were longer and there was no appreciable effect on the heart beats.

12.18.—350 c.c. saline solution were very rapidly given via the femoral vein at the rate of 100 c.c. per minute. The blood-pressure went up rapidly but unevenly to 100 mm., and fell to 88 mm. at 12.21.

12.23.—Control. Blood-pressure, 100 mm. The heart beats were slower, more regular, and much more powerful.

12.25.—Control. Blood-pressure, 106 mm. $\frac{1}{150}$ grain of strychnin (0.04 mgm. per kilo) given as before. The character of the tracing was spoiled by a partial obstruction of the cannula by a clot in the carotid artery.

12.47.—Blood-pressure, 98 mm. With the fall in pressure the heart beats were somewhat less forceful and somewhat irregular. The strychnin had no apparent effect. Cardiac failure rapidly ensued.

Summary.—(1) In a dog with high initial blood-pressure the pressure fell uniformly during the loss of about three fourths of the total amount of blood at a regular but rapid rate. The greatest fall occurred after the loss of the first one third of the blood. (2) Strychnin in therapeutic dose did not produce a rise of pressure either before or after the injection of normal saline solution. (3) Saline solution in amount equal to the amount of blood lost was begun to be rapidly injected eighteen minutes after the hemorrhage stopped. It caused a rapid rise in the blood-pressure, but brought it up to barely one half the original height. This level was sustained for only twenty minutes with temporary improvement of the pulse wave, and death rapidly followed from cardiac failure.

EXPERIMENT 26

Hemorrhage; Strychnin; Normal Saline Infusion

August 18, 1904.

Mongrel skye terrier dog; weight, 10 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

4.05.—Control on drum. Blood-pressure, 148 mm.

4.14.—Bleeding was begun at the same rate as in the preceding experiment. Blood-pressure, 138 mm. (femoral cannula).

4.20.—225 c.c. of blood removed. Blood-pressure, 68 mm. The fall was of the same character as in the preceding experiment.

4.21.—Control. Bled again. Total amount of blood removed, 300 c.c. Blood-pressure, 50 mm.

4.29.—Blood-pressure, 54 mm.

4.29½.—A dose of $\frac{1}{100}$ grain strychnin (0.06 mgm. per kilo) injected into the external jugular vein produced continuous general twitchings with periodic convulsions of short duration. The respirations were only slightly affected. The blood-pressure rose rapidly and steadily to 168 mm. in about two minutes. At this point the convulsions practically ceased and the blood-pressure gradually fell to 90 mm. at 4.39.

4.40.—Control. Blood-pressure, 62 mm. Artificial respiration was necessary. The ether was stopped.

4.45.—Ether still discontinued. Artificial respiration stopped. The blood-pressure rose to 86 mm., but immediately fell, with artificial respiration necessary at the beginning of the fall.

4.53.—Stopped the drum. The blood-pressure rose to 110 mm. and was maintained for eight minutes. The respirations were spasmodic, and at the rate of two per minute.

5.02.—Control. The blood-pressure fell from 86 mm. to 72 mm. during the minute which the control lasted. The ether was stopped.

5.03½.—With the continuance of the ether the blood-pressure rose to 92 mm.

5.15.—The respirations were 120 per minute. Blood-pressure, 92 mm.

5.36.—Blood-pressure, 92 mm. With $\frac{1}{100}$ grain more strychnin (0.06 mgm. per kilo) there was no rise in the pressure. There were two convulsions.

5.39.—$\frac{1}{50}$ grain strychnin (0.12 mgm. per kilo) caused marked convulsions, but no rise in the blood-pressure, which was at 82 mm.

5.44.—On rapidly giving 300 c.c. normal saline solution the blood-pressure rose to 120 mm., but this level was held for a few minutes only. Burning a paw, manipulating the sciatic nerve, and clamping the trachea had no effect on the blood-pressure.

Summary.—(1) With rapid hemorrhage (about one third the total amount of blood) a relatively much greater fall of the blood-pressure occurred after the removal of the first third of the blood. (2) In a dog with low initial blood-pressure a double therapeutic dose of strychnin given eight minutes after stopping the hemorrhage produced much more than the usual effect, the blood-pressure going 20 mm. higher than it was at the beginning of the experiment. The blood-pressure reached its original level in ten minutes, and then the heart was overtaxed. (3) The administration of a double therapeutic dose of strychnin was followed by respiratory failure, a regular heart action, and variable blood-pressure after temporary improvement, although after fifty minutes the blood-pressure was 30 mm. higher than when the bleeding was stopped, and at a fairly steady level. (4) After overaction of the vasomotor centers due to strychnin, the drug in almost tetanic dose produced convulsions, but had no effect on the blood-pressure. (5) Normal saline solution in amount equal to the amount of blood lost in an animal exhausted by strychnin-induced compensation had a very temporary effect, and one which was less than usual. The strychnin-induced compensation exhausted the vasomotor centers, and they failed to react to peripheral stimulation after the effect had worn off.

EXPERIMENT 27

Hemorrhage; Strychnin; Normal Saline Infusion

August 20, 1904.

Yellow mongrel dog; weight, 9.3 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.35.—Control on drum. Blood-pressure, 180 mm.

10.40.—Began to bleed.

10.42.—200 c.c. blood removed. Blood-pressure, 106 mm.

10.48.—300 c.c. blood removed. Blood-pressure, 46 mm. There was practically a continuous fall, which was more rapid with the second 100 c.c. of blood removed.

10.53.—Began to bleed again slowly. Blood-pressure, 56 mm.

10.55.—Total amount of blood removed, 555 c.c. There was a steady fall of the blood-pressure to 36 mm.

11.00.—Control. Blood-pressure, 56 mm. The heart action was more rapid, irregular, and less forceful. The respiratory wave was diminished one third.

11.00½.—$\frac{1}{100}$ grain strychnin (0.07 mgm. per kilo) was given intravenously. There was no effect in two minutes.

11.02½.—The same dose was repeated, and the blood-pressure slowly rose to 56 mm.

11.10.—Control. Blood-pressure, 60 mm. The pulse wave was distinctly longer, and the rate was more regular.

11.10½.—$\frac{1}{50}$ grain strychnin (0.13 mgm. per kilo) was given. Extreme convulsions were produced, which were not, however, characterized by the usual rise of pressure. The mean pressure throughout averaged 55 mm., with rapid respiratory failure occurring shortly, followed by cardiac failure.

11.20.—Recovery was brought about by artificial respiration, and 300 c.c. of normal saline solution were rapidly administered. The blood-pressure rose rapidly to 70 mm. and fell to 40 mm.

11.30.—Control. Blood-pressure, 80 mm.

11.41.—Blood-pressure averages 48 mm. On burning the paw there was no reaction. Death occurred.

Summary.—(1) The fall in blood-pressure was more uniform, with a slower rate of bleeding, than in the previous experiment (100 c.c. in two and two thirds minutes). (2) A double therapeutic dose of strychnin failed to produce the characteristic rise of blood-pressure after removal of about one half the total amount of blood, while a convulsive dose had but little effect on the blood-pressure level, but produced violent overaction of the heart. (3) Normal saline solution with artificial respiration brought slight and only momentary recovery —the animal with cardiac and vasomotor center exhaustion not reacting to stimulation after hemorrhage and strychnin in convulsive dose.

EXPERIMENT 28

Hemorrhage; Strychnin; Normal Saline Infusion

AUGUST, 1904.

Young bull terrier; weight, 12 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

1.45.—Control on drum.

1.50.—Began to bleed. Blood-pressure, 120 mm.

1.52½.—Blood-pressure, 88 mm.

1.55.—350 c.c. blood removed. The blood-pressure fell gradually to 84 mm., but the fall was more marked in the first half of the period of bleeding. The bleeding was allowed to continue.

2.02½.—Control. 60 c.c. blood removed. Blood-pressure, 70 mm.

2.06.—Blood-pressure the same.

2.20.—Blood-pressure, 66 mm.

2.32.—Began to bleed again. 70 c.c. more blood removed—total amount 480 c.c. Blood-pressure, 46 mm.

2.44.—Bled 50 c.c. Blood-pressure, 32 mm.

2.50.—Cardiac and respiratory failure occurred. 50 c.c. of normal saline solution were given intravenously. Artificial respiration was begun.

2.56.—$\frac{1}{50}$ grain strychnin (0.10 mgm. per kilo) was given intravenously. There was a slight momentary rise in blood-pressure, followed by a return to the same level (23 mm.), and this level was maintained until death occurred.

3.05.—Death occurred.

3.06.—100 c.c. normal saline solution given intravenously.

3.08.—100 c.c. more saline solution given, with no effect (total amount, 200 c.c.).

Summary.—(1) A double therapeutic dose of strychnin had no effect on an animal exhausted by continuous bleeding with removal of about one half the total amount of blood. (2) The blood-pressure fell unevenly with a rapid, regular rate of bleeding. (3) In a dog with low initial blood-pressure, normal saline solution administered intravenously fifty minutes after removal of the greater bulk of the blood, and ten minutes after a double therapeutic dose of strychnin, had no effect.

EXPERIMENT 29

Hemorrhage; Normal Saline Infusion; Rubber Bandage; Strychnin

September 12, 1904.

Mongrel dog; weight, 10 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

1.40.—Control on drum. Blood-pressure, 138 mm. The femoral cannula was put in place, and the sciatic nerve was exposed.

1.51.—Blood-pressure, 124 mm. Began to bleed.

1.55.—Blood-pressure, 106 mm. 100 c.c. blood removed.

1.58.—Blood-pressure, 84 mm. 100 c.c. blood removed.

2.02.—Blood-pressure, 50 mm. 100 c.c. blood removed.

2.04.—Blood-pressure, 35 mm. 100 c.c. blood removed.

2.08.—Blood-pressure, 36 mm. 50 c.c. blood removed (total amount, 450 c.c.).

2.09.—A paw was burned.

2.10.—The sciatic nerve was manipulated.

2.11.—The larynx was manipulated.

2.12.—Blood-pressure, 47 mm. There was a steady rise in the pressure during the last four minutes, and the above procedures had no effect on it. The manipulation of the larynx inhibited the respiration for a moment.

2.13¼.—Blood-pressure, 43 mm. On burning a paw it rose 12 mm.

2.14½.—On burning a paw there was no effect on the pressure.

2.15½.—Began the intravenous injection of normal saline solution. Blood-pressure, 40 mm.

2.17.—50 c.c. saline solution given.

2.18.—50 c.c. saline solution given. Blood-pressure, 66 mm. Stopped the saline injection.

2.20.—Blood-pressure, 74 mm. Started the saline injection.

2.22½.—Blood-pressure, 85 mm. 100 c.c. saline solution given.

2.24½.—Blood-pressure, 86 mm. 100 c.c. saline solution given.

2.28.—Blood-pressure, 86 mm. 100 c.c. saline solution given.

2.29½.—Blood-pressure, 88 mm. 50 c.c. saline solution given (total amount up to this point, 450 c.c.).

2.30½.—On burning a paw there was a rise of blood-pressure of 6 mm.

2.31½.—On stimulating the sciatic nerve there was an initial fall of pressure, and the subsequent rise did not exceed the original level.

2.32½.—On manipulating the larynx there was a fall of pressure of 15 mm.

2.33.—Blood-pressure, 78 mm. A rubber bandage was applied over the legs and abdomen to raise the pressure.

2.41½.—Blood-pressure, 97 mm.

2.52.—Blood-pressure, 99 mm.

2.55.—Blood-pressure, 99 mm.

3.00.—Blood-pressure, 71 mm.

3.02½.—Blood-pressure, 85 mm.

3.05.—Blood-pressure, 86 mm.

3.06.—On burning a paw there was a rise in pressure of 13 mm.

3.07.—On stimulating the sciatic nerve there was an initial fall in pressure and a return to the former level only.

3.08.—On manipulating the larynx there was a slight fall of the pressure, and the respiration was partially inhibited.

3.10½.—Blood-pressure, 93 mm. $\frac{1}{150}$ grain strychnin (0.04 mgm. per kilo) was given intravenously.

3.13.—Blood-pressure, 85 mm. The dose of strychnin was repeated.

3.15.—Blood-pressure, 90 mm.

3.19.—Blood-pressure, 88 mm. Began to inject normal saline solution intravenously.

3.26.—Blood-pressure, 97 mm. 100 c.c. saline solution given.

3.33.—Blood-pressure, 96 mm. 100 c.c. saline solution given.

3.46.—Blood-pressure, 81 mm.

3.48.—Blood-pressure, 78 mm. On stimulating the sciatic nerve there was a very slight fall of pressure.

Summary.—(1) On removing about three fifths the total amount of blood the greatest relative fall in the blood-pressure occurred during taking out the second third of the blood. (2) Peripheral stimulation within five minutes after the bleeding stopped produced a very variable reaction. (3) The fairly rapid intravenous injection of normal saline solution in amount equal to the quantity of blood removed—begun seven minutes after stopping the bleeding—increased the pulse wave beyond the initial height, and raised the blood-pressure to one half the original height. This level was maintained until the dog was killed, seventy-five minutes after the end of the infusion. (4) After the intravenous injection of normal saline solution the reaction to peripheral stimulation was much more marked. (5) The use of the rubber bandage after the saline infusion gave a decidedly and uniformly higher level of blood-pressure. (6) The injection of a double therapeutic dose of strychnin after the saline infusion did not cause a rise in the blood-pressure. At this time the reaction to peripheral stimulation was more marked than it was just after the infusion. An excess of saline solution over the amount of blood removed caused only a temporary rise in pressure, and the heart quickly became more irregular.

EXPERIMENT 30

Hemorrhage; Normal Saline Infusion; Strychnin; Rubber Bandage; Adrenalin

SEPTEMBER 14, 1904.

Mongrel; weight, 14.5 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

2.57.—Blood-pressure, 159 mm.

3.24½.—Blood-pressure, 127 mm. The femoral cannula was put in place.

3.27.—Began to bleed.

3.31.—100 c.c. blood removed. Blood-pressure, 96 mm.

3.35.—100 c.c. blood removed. Blood-pressure, 77 mm. The compensation was good at each control.

3.39.—100 c.c. blood removed. Blood-pressure, 70 mm.

3.44.—110 c.c. blood removed. Blood-pressure, 63 mm.

3.48.—90 c.c. blood removed. Blood-pressure, 62 mm.

3.52.—100 c.c. blood removed. Blood-pressure, 40 mm. On burning a paw there was a rise of pressure of 9 mm.

3.55.—There was a slight compensation. 65 c.c. more blood were removed (total, 665 c.c.). Blood-pressure, 46 mm.

3.56.—On burning a paw there was a rise of pressure of 6 mm. On stimulating the sciatic nerve there was a slight fall, and then a recovery to the former level.

4.00.—Blood-pressure, 45 mm. Began to inject normal saline solution intravenously.

4.13.—Blood-pressure, 88 mm. The rise of pressure to this point was steady, and followed the injection of 400 c.c. of saline solution (at the rate of 100 c.c. in three and a quarter minutes).

4.15.—Control. Blood-pressure, 92 mm.

4.18.—100 c.c. saline solution injected (total amount, 500 c.c.). Blood-pressure, 92 mm.

4.23.—On burning a paw there was a rise of pressure of 18 mm. On immediately repeating there was a rise of 14 mm.

4.26.—Blood-pressure, 100 mm. $\frac{1}{150}$ grain strychnin (0.03 mgm. per kilo) was given intravenously in 5 c.c. of saline solution. There was a temporary fall in the blood-pressure. Accidental asphyxia occurred, followed by a rise and then a fall in the blood-pressure, and recovery.

4.34.—Blood-pressure, 110 mm.

4.35.—Control. Blood-pressure, 108 mm. Application of the rubber bandage had no effect in raising the blood-pressure, but when it was removed it fell to 81 mm.

4.40.—4 drops of adrenalin chlorid solution (1–1,000) were given in 10 c.c. normal saline solution. There was a sudden rise in the pressure to 159 mm., which was not maintained, but fell to 62 mm. in three minutes.

4.55.—Blood-pressure, 60 mm.

5.00.—Blood-pressure, 64 mm.

5.05.—Blood-pressure, 64 mm. The pulse was thready and the heart action feeble. The dog was killed.

Summary.—(1) In a dog which compensated markedly in the course of a hemorrhage, peripheral stimulation evoked little reaction and did not raise the blood-pressure to a higher level, and there was no further compensation in the two minutes before the saline infusion was started. (2) The infusion of normal saline solution at the rate of 100 c.c. in three minutes brought back the blood-pressure half way to the initial level, but the heart was overtaxed somewhat during the latter part of the infusion. (3) Peripheral stimulation had much more effect after the infusion. (4) A small therapeutic dose of strychnin caused some rise in the blood-pressure when given when the pressure began to fall after the infusion, but this was followed by a further fall in a few minutes. (5) A rubber bandage, applied when the pressure was falling after the infusion, and a therapeutic dose of strychnin, only maintained the pressure, and did not raise it.

EXPERIMENT 31

Hemorrhage; Oxygenated Locke's Solution; Strychnin

September 19, 1904.

Mongrel dog; weight, 11 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

3.00.—Control on drum.

3.10.—Began to bleed. Blood-pressure, 130 mm.

3.15.—100 c.c. blood removed. Blood-pressure, 122 mm.

3.20.—100 c.c. blood removed. Blood-pressure, 101 mm.

3.25.—100 c.c. blood removed. Blood-pressure, 72 mm.

3.30.—150 c.c. blood removed. Blood-pressure, 60 mm.

3.35.—Began to bleed again. 60 c.c. blood removed (total amount, 410 c.c.). Blood-pressure, 35 mm. On burning a paw there was a rise of pressure of 5 mm.

3.41½.—Began to inject oxygenated Locke's solution into the femoral vein.

3.45.—100 c.c. solution injected. Blood-pressure, 65 mm.

3.47½.—100 c.c. solution injected. Blood-pressure, 94 mm.

3.51.—100 c.c. solution injected.

3.54.—100 c.c. solution injected. Blood-pressure, 112 mm.

4.01½.—100 c.c. solution injected. Blood-pressure, 96 mm. The level was not maintained.

4.03.—100 c.c. solution injected (total amount, 600 c.c.). Blood-pressure, 110 mm.

4.11.—Blood-pressure, 98 mm.

4.14.—Control. On burning a paw there was a rise of pressure of 19 mm. The heart beat was stronger.

4.16½.—Control. $\frac{1}{150}$ grain strychnin (0.04 mgm. per kilo) was given intravenously.

4.20.—Blood-pressure, 98 mm.

4.23.—Control. The dose of strychnin was repeated. Blood-pressure, 94 mm.

4.25.—Control. Blood-pressure, 92 mm.

4.29.—Repeated the dose of strychnin in the jugular vein.

4.29½.—On burning a paw there was a less marked reaction than at the previous time.

4.32.—Control. Blood-pressure, 102 mm. A total of 0.12 mgm. strychnin was in the circulation at this time.

Summary.—(1) After the hemorrhage oxygenated Locke's solution, in amount equal to the amount of blood removed, was immediately begun to be injected intravenously at the rate of about 100 c.c. in three minutes, and brought the blood-pressure back within 10 mm. of the original level, but further infusion was associated with lowering of the pressure. The heart was not overtaxed by the amount given. (2) The reaction after hemorrhage to peripheral stimulation was more marked after saline infusion. (3) A therapeutic dose of strychnin after hemorrhage and saline infusion did not raise the blood-pressure, and the vasomotor centers showed even less activity after its administration than before. (4) The same was true of the nerve centers after three times the therapeutic dose of strychnin, but the blood-pressure level was raised appreciably.

EXPERIMENT 32

Hemorrhage; Locke's Solution; Strychnin

September 15, 1904.

Fox terrier dog; weight, 8.2 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.45.—Control on drum. Blood-pressure, 124 mm. The femoral cannula was put in place and the sciatic nerve exposed.

10.50.—Blood-pressure, 145 mm.

10.51.—Began to bleed.

10.55.—100 c.c. blood removed. Blood-pressure, 114 mm.

10.59.—100 c.c. blood removed. Blood-pressure, 92 mm.

11.04.—Respiratory failure occurred, and artificial respiration was given.

11.10.—150 c.c. blood removed (total amount, 350 c.c.). Blood-pressure, 37 mm.

11.11.—On burning a paw there was no reaction. On stimulating the sciatic nerve there was no reaction.

11.13.—Blood-pressure, 43 mm. Began the intravenous injection of warm Locke's solution.

11.15.—100 c.c. Locke's solution injected. Blood-pressure, 62 mm.

11.18.—Artificial respiration was stopped, and the ether resumed.

11.19.—100 c.c. Locke's solution injected. Blood-pressure, 119 mm.

11.22½.—100 c.c. Locke's solution injected. Blood-pressure, 132 mm.

11.24.—50 c.c. Locke's solution injected. Blood-pressure, 135 mm.

11.29.—Blood-pressure, 124 mm.

11.34.—Blood-pressure, 112 mm.

11.34½.—Began to inject Locke's solution again.

11.36.—50 c.c. Locke's solution injected. Blood-pressure, 122 mm.

11.38.—50 c.c. Locke's solution injected (total amount, 450 c.c.). Blood-pressure, 130 mm.

11.43.—Blood-pressure, 115 mm. The fall was due to the ether.

11.48.—Blood-pressure, 127 mm.

11.50.—Blood-pressure, 121 mm.

11.50½.—Began to inject Locke's solution again.

11.51½.—On burning a paw there was a rise of pressure of 2 mm.

11.52.—Blood-pressure, 133 mm.

11.54.—Blood-pressure, 139 mm.

11.59.—Blood-pressure, 120 mm.

12.04.—Blood-pressure, 112 mm. The drop in each instance was apparently due to the ether.

12.09.—Blood-pressure, 112 mm.

12.14.—Blood-pressure, 116 mm.

12.15.—Blood-pressure, 110 mm. $\frac{1}{200}$ grain strychnin (0.04 mgm. per kilo) was given in 10 c.c. saline solution.

12.18.—Stopped the drum. Blood-pressure, 122 mm.

12.20.—Blood-pressure, 124 mm.

12.25.—Blood-pressure, 116 mm.

12.26.—Blood-pressure, 112 mm. On burning a paw there was a rise of pressure of 27 mm.

12.27½.—On stimulating the sciatic nerve there was a rise of pressure of 3 mm., and no initial fall.

Summary.—(1) In a hemorrhage of about one half the total amount of blood with slight compensation during the bleeding, failure of peripheral stimulation to evoke reaction was associated with absence of further compensation. (2) An infusion of Locke's solution of 100 c.c. larger quantity than the amount of blood removed was begun two minutes after the bleeding stopped, and given at the rate of 100 c.c. in four minutes, with the result that the blood-pressure was brought back to within a few millimeters of the original level, and practically maintained at this level for forty minutes. (3) After a therapeutic dose of strychnin after hemorrhage and recovery by means of Locke's solution, which only temporarily raised the blood-pressure, peripheral stimulation was followed by an increased pressure, but subsequent stimulation was less effective.

EXPERIMENT 33

Hemorrhage; Oxygenated Locke's Solution; Adrenalin

September 20, 1904.

Mongrel dog; weight, 10 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

9.35.—Control on drum. Blood-pressure, 186 mm.

9.58.—Control. Blood-pressure, 172 mm. On burning a paw there was a rise of pressure of 33 mm.

10.00.—Began to bleed.

10.05.—Blood-pressure, 158 mm. 100 c.c. blood removed.

10.11.—Blood-pressure, 103 mm. 100 c.c. blood removed.

10.16.—Blood-pressure, 74 mm. 100 c.c. blood removed.

10.21.—Blood-pressure, 57 mm. 100 c.c. blood removed.

10.30.—Blood-pressure, 46 mm. 100 c.c. blood removed (total amount, 500 c.c.). On burning a paw, under light anesthesia, there was a rise of pressure of 19 mm. Control.

10.31.—Control. Blood-pressure, 93 mm.

10.35.—Control. Blood-pressure, 109 mm.

10.40.—Control. Blood-pressure, 122 mm. There was momentary asphyxia. The rise of pressure was sustained.

10.45.—Control. Blood-pressure, 138 mm.

11.00.—Control. Blood-pressure, 112 mm.

11.15.—Control. Blood-pressure, 90 mm.

11.30.—Control. Blood-pressure, 91 mm. There was momentary asphyxia.

11.45.—Control. Blood-pressure, 70 mm.

12.00.—Control. Blood-pressure, 76 mm. On burning a paw there was a rise of 5 mm.

12.16½.—Stopped the drum. Asphyxia occurred from the anesthetic.

12.17½.—Control. Blood-pressure, 64 mm.

12.19.—Began to inject oxygenated Locke's solution intravenously.

12.21.—Owing to an accident to the apparatus only a small amount of solution reached the circulation.

12.26.—Began to inject again.

12.28½.—100 c.c. solution injected. Blood-pressure, 107 mm.

12.32.—100 c.c. solution injected. Blood-pressure, 126 mm.

12.35½.—100 c.c. solution injected. Blood-pressure, 126 mm. Temporary asphyxia occurred.

12.41.—100 c.c. solution injected. Blood-pressure, 142 mm.

12.45.—100 c.c. solution injected (total amount, 500 c.c.). Blood-pressure, 141 mm.

12.53.—A clot was removed from the carotid cannula.

12.55.—Artificial respiration was begun, as sudden cardiac and respiratory failure occurred. One minim of 1–1,000 adrenalin chlorid solution had no effect.

Autopsy.—The gut wall was very edematous. The lymphatics and veins were engorged. The other viscera, especially the pancreas, were very edematous. The heart was dilated and engorged.

Summary.—(1) After hemorrhage good reaction to peripheral stimulation was associated with extremely marked compensation. (2) Spontaneous failure of compensation was associated with diminished reaction to peripheral stimulation. (3) After a long wait, on infusing oxygenated Locke's solution in amount equal to the amount of blood removed at a rate of 100 c.c. in three minutes, the blood-pressure was brought back to two thirds of the original level, but the respiration was markedly embarrassed, and the heart was overtaxed before one half the solution was in, and cardiac and respiratory failure resulted. (3) Adrenalin had no effect after cardiac failure following infusion of Locke's solution.

EXPERIMENT 34

Hemorrhage; Locke's Solution; Strychnin

SEPTEMBER, 1904.

Mongrel dog; weight, 5 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

9.47.—Control on drum. Blood-pressure, 125 mm.

10.00.—Control. Blood-pressure, 101 mm. Began to bleed.

10.10.—100 c.c. blood removed. Blood-pressure, 57 mm.

10.13.—50 c.c. blood removed. Blood-pressure, 47 mm. A clot was removed from the carotid cannula.

10.14.—Control. Began to bleed again. Blood-pressure, 62 mm.

10.17.—50 c.c. blood removed (total amount, 200 c.c.). Artificial respiration was begun.

10.19.—Artificial respiration was stopped. Blood-pressure, 34 mm.

10.20.—Control.

10.24 to 10.25.—Artificial respiration was given.

10.30.—Control. Blood-pressure, 35 mm.

10.35.—Artificial respiration was resumed. Blood-pressure, 29 mm.

11.05.—Control. Blood-pressure, 15 mm.

11.05½.—On burning a paw there was no reaction.

11.01.—Began to inject Locke's solution (non-oxygenated) intravenously.

11.04.—100 c.c. solution injected. Blood-pressure, 48 mm.

11.08.—100 c.c. solution injected (total amount up to this point, 200 c.c.). Blood-pressure, 67 mm. The artificial respiration was stopped.

11.08½.—Control.

11.15.—Control. Blood-pressure, 47 mm.

11.22.—Began to inject Locke's solution again. Blood-pressure, 43 mm.

11.24.—50 c.c. solution injected. Blood-pressure, 58 mm.

11.25.—Blood-pressure, 54 mm.

11.20.—Control. Blood-pressure, 44 mm. Strychnin in dose of 0.08 mgm. per kilo was injected into the femoral vein in 5 c.c. of Locke's solution.

11.33.—Control. Blood-pressure, 35 mm. The dose of strychnin was repeated.

11.35.—Artificial respiration was resumed.

11.40.—Control. Blood-pressure, 31 mm. On burning a paw there was no reaction.

11.43.—Control. Blood-pressure, 29 mm. A double dose of strychnin was given. There was a temporary rise of pressure from the injection of a few cubic centimeters of Locke's solution. The total amount of strychnin of 0.32 mgm. per kilo had no effect.

11.48.—Death occurred.

Summary.—(1) In a dog with low initial blood-pressure (indicating inactivity of the vasomotor centers), and cardiac failure from hemorrhage, non-oxygenated Locke's solution injected at once, at the rate of 100 c.c. in four minutes, and in amount equal to the amount of blood removed, brought the blood-pressure back to one half the original level, but only momentarily, and further infusion had a similar effect with a relatively greater subsequent fall. (2) With low initial blood-pressure a tetanic dose of strychnin in divided amounts after hemorrhage, cardiac failure, recovery with Locke's solution, and subsequent fall of pressure had no effect. The blood-pressure level at the first administration of the strychnin was 44 mm.

EXPERIMENT 35

Hemorrhage; Strychnin; Digitalin

August 24, 1904.

Fox terrier bitch; weight, 8 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

3.50.—Control on drum. Blood-pressure, 160 mm.

3.55.—Began to bleed.

4.00.—100 c.c. blood removed. Blood-pressure, 148 mm.

4.06.—100 c.c. blood removed. Blood-pressure, 98 mm.

4.10.—10 c.c. blood removed. There was a rise of a few millimeters in the blood-pressure.

4.22.—40 c.c. blood removed (total amount, 250 c.c.). Blood-pressure, 52 mm. The corneal reflex could not be obtained. The respirations were good.

4.24.—A paw was burned, and there was a temporary rise in the blood-pressure to 60 mm.

4.29½.—The pressure fell to its former level of 52 mm. Artificial respiration was used.

4.40.—Blood-pressure, 64 mm.

4.49.—A paw was burned with a resulting depressor effect, the blood-pressure falling to 46 mm.

4.52.—On manipulating the sciatic nerve there was a slight depressor effect.

4.58.—Electric stimulation of the sciatic nerve caused a more marked depressor effect.

5.01.—Blood-pressure, 78 mm.—a compensatory rise of 26 millimeters.

5.04.—Blood-pressure, 64 mm.

5.05.—$\frac{1}{80}$ grain of strychnin (0.10 mgm. per kilo) was given intravenously. Slight tremors occurred, and the respirations were increased.

5.07.—There was a slight convulsive movement, but no rise in the blood-pressure.

5.15.—Electric stimulation of the sciatic nerve caused a fall of pressure, just as it did before the strychnin was given.

5.20.—$\frac{1}{75}$ grain digitalin (0.10 mgm. per kilo) was given intravenously.

5.30.—Cardiac and respiratory failure occurred. Artificial respiration brought back the heart action.

5.35.—Control. Blood-pressure, 42 mm. There was no effect apparent from the digitalin.

5.36.—$\frac{1}{50}$ grain digitalin (0.16 mgm. per kilo) was given intravenously. Stimulating the sciatic nerve had a very slight depressor effect, and burning the paw had no effect at all. A second stimulation of the sciatic nerve had no effect.

5.48.—$\frac{1}{75}$ grain digitalin (0.10 mgm. per kilo), given intravenously, was followed in two minutes by death.

Summary.—(1) The height of compensation after stopping the hemorrhage was reached in forty-one minutes, and was only sustained for a few minutes. It was associated with fairly active reaction of the vasomotor centers to peripheral stimulation. (2) Double therapeutic doses of strychnin produced more than the usual symptomatic effect, but the blood-pressure was not affected. Its administration together with a small dose of digitalin was soon followed by cardiac failure. (3) Stimulation of the sensory nerves immediately after bleeding produced much less effect than usual, and after some time only a depressor effect of lessened degree. After the strychnin there was the same effect, which vanished altogether in thirty minutes. (4) A therapeutic dose of digitalin given one hour after the bleeding slowly affected the

heart, without causing rise of blood-pressure, and apparently hastened death.

EXPERIMENT 36

Hemorrhage; Digitalin; Strychnin; Adrenalin

August 25, 1904.

Mongrel dog; weight, 7.3 kilos. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

4.15.—Control on drum. Blood-pressure, 146 mm. The femoral cannula was put in place.

4.35.—Control. Began to bleed.

4.45.—Bled 250 c.c. Blood-pressure, 36 mm.

5.00.—Control. There was marked compensation, the blood-pressure rising to 62 mm. $\frac{1}{64}$ grain digitalin (0.13 mgm. per kilo) was given intravenously.

5.14.—Blood-pressure, 74 mm. The rise in pressure was gradual, and the effect of the digitalin was not apparent.

5.15.—Began to bleed.

5.16.—Removed 100 c.c. more blood. Blood-pressure, 42 mm.

5.17.—Control. Blood-pressure, 48 mm.

5.30.—Control. Bled 50 c.c. (total, 400 c.c.). Blood-pressure, 30 mm.

5.35.—Control. 0.2 mgm. per kilo strychnin was given intravenously. Convulsions appeared, and it was necessary to use artificial respiration.

5.40.—100 c.c. 1–50,000 solution of adrenalin chlorid were given intravenously. The maximum point reached by the blood-pressure was 110 mm. The minimum blood-pressure was 20 mm. The length of the stroke of the recording style was 90 mm.

5.55.—50 c.c. of 1–50,000 adrenalin given intravenously was followed by rapid death.

Summary.—(1) A therapeutic dose of digitalin given to a dog with poor compensation had no apparent effect except to slow the heart rate somewhat, and did not help to maintain the level of the compensation. (2) Strychnin in convulsive doses failed to raise the blood-pressure except during a spasm, and was quickly followed by cardiac failure. (3) Although adrenalin enormously increased the pulse wave, it raised the blood-pressure but slightly, and was quickly followed by cardiac failure.

EXPERIMENT 37

Hemorrhage; Digitalin; Strychnin; Adrenalin

AUGUST 26, 1904.

Black mongrel; weight, 16 kilos. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

3.10.—Control on drum. Blood-pressure, 182 mm.

3.25.—Began to bleed.

3.36.—415 c.c. blood removed. Blood-pressure, 54 mm.

3.38.—10 c.c. blood removed. Blood-pressure, 62 mm.

3.43.—Control.

3.46.—Control. 0.07 mgm. per kilo digitalin given intravenously.

3.48½.—Stopped the drum. Blood-pressure, 80 mm. No effect was apparent from the digitalin.

3.54.—The dose of digitalin was repeated. The respirations were increased. Blood-pressure, 86 mm.

4.10.—Blood-pressure, 98 mm. No effect was apparent from the digitalin. The respirations were still stronger.

4.23.—Control. Blood-pressure, 102 mm.

4.27.—Control. 75 c.c. blood removed. Blood-pressure, 98 mm.

4.32.—Control. 75 c.c. blood removed. Blood-pressure, 64 mm.

4.38.—Control. 75 c.c. blood removed. Blood-pressure, 67 mm.

4.42.—Blood-pressure, 60 mm.

4.55.—Control. 35 c.c. blood removed (total amount, 685 c.c.). Blood-pressure, 62 mm.

5.04.—Blood-pressure, 56 mm. 0.08 mgm. per kilo strychnin given intravenously. Artificial respiration was started.

5.08.—Blood-pressure, 40 mm. 100 c.c. 1–50,000 adrenalin chlorid solution was rapidly given intravenously, and then 100 c.c. more was given slowly. The effect was marked, but temporary.

5.15.—Death occurred.

Summary.—(1) The height of compensation was reached in thirty minutes after partial exsanguination. (2) After large exsanguination a double therapeutic dose of strychnin had no effect on the blood-pressure. (3) Adrenalin chlorid solution increased the pulse wave, but raised the mean blood-pressure relatively little, and was followed by cardiac failure.

EXPERIMENT 38

Hemorrhage; Digitalin; Adrenalin

August 26, 1904.

Bull dog; weight, 19 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

2.13.—Control on drum. Blood-pressure, 158 mm.

2.25.—Control. Began to bleed.

2.45.—Control. 625 c.c. blood removed. Blood-pressure, 70 mm. The respiration was good. The anesthesia was light.

3.43.—Control. Blood-pressure, 52 mm.

3.46.—Control. Digitalin, 0.06 mgm. per kilo, was injected into the external jugular vein.

3.46½.—Stopped the drum.

3.54.—The dose of digitalin was repeated in the right femoral vein. Respiratory failure occurred.

4.04.—Artificial respiration was begun. Blood-pressure, 54 mm. There was no digitalin effect apparent.

4.05.—Control. Blood-pressure, 50 mm.

4.10.—150 c.c. of 1–50,000 adrenalin chlorid solution was given intravenously, and was ineffectual.

4.15.—The heart was massaged, and more adrenalin solution was given slowly.

Summary.—(1) Digitalin given in repeated dose after hemorrhage did not raise the blood-pressure, and respiratory failure occurred. (2) On giving artificial respiration the infusion of adrenalin in saline solution did not raise the blood-pressure materially, and death followed.

EXPERIMENT 39

Hemorrhage; Digitalin; Adrenalin

August 25, 1904.

Mongrel dog; weight, 6 kilos; condition, good. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

3.40.—Control on drum. Blood-pressure, 120 mm.

3.44.—Began to bleed.

3.46.—Control. 110 c.c. blood removed. Blood-pressure, 46 mm.

3.48½.—Control. 100 c.c. blood removed (total amount, 210 c.c.). Asphyxia developed, and artificial respiration was used.

4.30.—Control. Ether resumed. Natural breathing began. Blood-pressure, 68 mm.

5.00.—Control. $\frac{1}{60}$ grain digitalin (0.18 mgm. per kilo) was given intravenously. Blood-pressure, 70 mm. Artificial respiration was begun again. The effect of the digitalin was quickly apparent, and was followed by gradual cardiac failure, and death. The injection of 40 c.c. of 1–50,000 solution of adrenalin chlorid into the femoral vein was ineffectual.

Summary.—The loss of about two fifths of the total blood was followed by good compensation. A therapeutic dose of digitalin was then quickly followed by cardiac failure.

EXPERIMENT 40

Hemorrhage; Digitalin; Locke's Solution; Strychnin; Adrenalin

SEPTEMBER 19, 1904.

Mongrel; weight, 9.5 kilos. The general condition was good, but the heart beat was very weak. The blood-pressure was 148 mm. Ether anesthesia through tracheal cannula. Other arrangements as in Experiment 1.

10.38.—Began to bleed.

10.43.—Control on drum. Blood-pressure, 124 mm. On burning a paw there was a rise of pressure of 21 mm.

10.45.—Began to bleed.

10.50.—200 c.c. blood removed. Blood-pressure, 97 mm. $\frac{1}{150}$ grain (0.04 mgm. per kilo) digitalin was given intravenously.

10.54.—Blood-pressure, 85 mm. Began to bleed again.

10.56.—50 c.c. blood removed. Blood-pressure, 68 mm.

10.59.—50 c.c. blood removed. Blood-pressure, 49 mm.

11.04.—100 c.c. blood removed (total amount, 400 c.c.). Blood-pressure, 37 mm.

11.06.—Blood-pressure, 36 mm. Burning a paw was followed by a gradual slight rise of pressure.

11.10.—Blood-pressure, 38 mm. The intravenous injection of Locke's solution was begun.

11.15.—100 c.c. solution injected. Blood-pressure, 54 mm. There was marked improvement in the heart action.

11.17.—100 c.c. solution injected. Blood-pressure, 74 mm.

11.19.—100 c.c. solution injected. Blood-pressure, 86 mm.

11.21.—100 c.c. solution injected. Blood pressure, 94 mm.

11.23½.—100 c.c. solution injected. Blood-pressure, 100 mm.

11.26½.—100 c.c. solution injected (total amount, 600 c.c.). Blood-pressure, 106 mm.

11.31½.—Blood-pressure, 110 mm. The heart showed moderate effects from the digitalin, the rate was slowed, and the beat strong.

11.36.—Blood-pressure, 105 mm. On burning a paw there was a rise of pressure of 3 mm.

11.45.—$\frac{1}{150}$ grain strychnin (0.045 mgm. per kilo) was injected into the jugular vein. The dose was not a full one.

11.45½.—The dose was repeated.

11.50.—Blood-pressure, 104 mm.

11.53½.—Blood-pressure, 104 mm.

11.54.—Repeated the dose of strychnin again.

11.56.—Blood-pressure, 103.5 mm. On burning a paw there was a slight initial fall in pressure, but no subsequent rise. This was repeated in one minute with the same effect.

12.02.—Blood-pressure, 98 mm. The injection of Locke's solution was begun again.

12.05.—100 c.c. solution injected. Blood-pressure, 102 mm.

12.10.—Blood-pressure, 98 mm. The injection of 3 minims of adrenalin chlorid solution caused a rise of pressure of 40 mm., which was followed by a fall. On slowly giving 8 minims more the pressure was held at the level of 90 mm. The dog was killed.

Summary.—(1) In a dog with a feeble running pulse and low initial blood-pressure, failure to react to peripheral stimulation after hemorrhage was associated with failure to compensate. (2) The intravenous injection of Locke's solution, begun four minutes after the hemorrhage stopped, at the rate of 100 c.c. in two minutes, and in amount one third more than the amount of blood removed, brought back the blood-pressure to five sixths of the original level, and maintained it well. The heart, however, was temporarily overtaxed, but slowly recovered its normal rhythm. (3) A double therapeutic dose of strychnin after hemorrhage and infusion of Locke's solution did not produce any rise of blood-pressure. (4) After hemorrhage, recovery by means of Locke's solution, and a triple therapeutic dose of strychnin, peripheral stimulation was followed by a depressor effect only.

EXPERIMENT 41

Dog A.—Hemorrhage; Digitalin; Strychnin. Dog B.—Digitalin; Strychnin

OCTOBER 3, 1904.

The dogs were of equal size, and weighed about 7 kilos each. Ether anesthesia for each through tracheal cannula. Other arrange-

ments as in Experiment 1, with both dogs recording on the same drum.

11.13.—Control on drum. Dog A.—Blood-pressure, 135 mm. Dog B.—Blood-pressure, 158 mm.

11.27.—Dog A.—Began to bleed. Blood-pressure, 130 mm. Dog B.—Blood-pressure, 132 mm.

11.32.—Dog A.—100 c.c. blood removed. Blood-pressure, 114 mm. Dog B.—Blood-pressure, 144 mm.

11.37.—Dog A.—100 c.c. blood removed. Blood-pressure, 86 mm. Dog B.—Blood-pressure, 121 mm.

11.42.—Dog A.—100 c.c. blood removed (total amount, 300 c.c.). Blood-pressure, 40 mm. Dog B.—Blood-pressure, 133 mm.

11.45.—Dog A.—Blood-pressure, 42 mm. $\frac{1}{60}$ grain digitalin (about 0.15 mgm. per kilo) was given in 10 c.c. normal saline solution in the femoral vein. Dog. B.—Blood-pressure, 144 mm. The same dose of digitalin was given in the same way.

11.59.—Dog A.—Blood-pressure, 67 mm. The heart beats were distinctly more regular, but there was no definite digitalin effect. Dog B.—Blood-pressure, 146 mm. There was no perceptible digitalin effect. Stopped the drum.

12.00.—Dog A.—Blood-pressure, 68 mm. Dog B.—Blood-pressure, 132 mm.

12.05.—Dog A.—Blood-pressure, 65 mm. $\frac{1}{150}$ grain strychnin (0.06 mgm. per kilo) was given intravenously in 10 c.c. normal saline solution. Dog B.—Blood-pressure, 122 mm.

12.10.—Dog A.—Repeated the dose of strychnin.

12.15.—Dog A.—Blood-pressure, 65 mm. Dog B.—Blood-pressure, 138 mm. Stopped the drum.

12.20.—Dog A.—Blood-pressure, 56 mm. Dog B.—Blood-pressure, 134 mm.

12.25.—Dog A.—Blood-pressure, 49 mm.. $\frac{1}{75}$ grain strychnin (0.12 mgm. per kilo) was given as before, and convulsions occurred. This was about three fourths of a tetanic dose for a 7-kilo dog. Dog B.—Gave same dose.

12.30.—Dog B.—$\frac{1}{20}$ grain strychnin was given (total dose of 4.0 mgm. per kilo). This was evidently a large overdose. Convulsions occurred.

Summary.—In a bled dog digitalin apparently had some slight effect in making the heart beats more regular, while in an unbled dog a similar dose had no apparent effect.

EXPERIMENT 42

Dog A.—Digitalin; Strychnin. Dog B.—Hemorrhage; Digitalin; Strychnin

SEPTEMBER, 1904.

Dog A.—Mongrel fox terrier; weight, 6.3 kilos; condition, good. Dog B.—Mongrel black and tan; weight, 6.3 kilos; condition, good. Ether anesthesia for each dog through tracheal cannula. Both dogs recorded on the same drum, and otherwise the arrangements were as in Experiment 1.

9.50.—Control. Dog A.—Blood-pressure, 108 mm. Dog B.—Blood-pressure, 190 mm.

10.04.—Control. Dog A.—Blood-pressure, 104 mm. Dog B.—Blood-pressure, 164 mm.

10.05.—Dog A.—Blood-pressure, 98 mm. Dog B.—Began to bleed.

10.15.—Dog B.—100 c.c. blood removed. Blood-pressure, 140 mm.

10.18.—Dog A.—Blood-pressure, 106 mm. Dog B.—100 c.c. blood removed (total amount, 200 c.c.). Blood-pressure, 30 mm.

10.34.—Dog A.—Blood-pressure, 114 mm. Dog B.—Blood-pressure, 34 mm. Both dogs were given $\frac{1}{60}$ grain digitalin (0.17 mgm. per kilo) in 10 c.c. normal saline solution. Dog B.—There was a slight rise of blood-pressure to 42 mm., which was maintained.

10.39.—Dog A.—Blood-pressure, 116 mm. Dog B.—Blood-pressure, 40 mm.

10.46.—The blood-pressure of each dog was unchanged.

10.50.—Control. Dog A.—Blood-pressure, 120 mm. Dog B.—Blood-pressure, 40 mm.

10.56.—Control. Dog B.—There was a slight fall in the pressure.

11.00.—Both dogs were given $\frac{1}{150}$ grain strychnin (0.06 mgm. per kilo). Dog A.—The pressure was raised. Dog B.—Blood-pressure, 38 mm.

11.01.—Dog B.—Artificial respiration was begun. The pressure was gradually falling. The dose of strychnin was repeated for both dogs, and some muscular twitchings occurred.

11.05.—On repeating the dose of strychnin again for both dogs the twitchings were more marked (total dose, 0.30 mgm. per kilo). Dog B.—Death quickly followed. Dog A.—The blood-pressure remained the same throughout.

Summary.—In a dog (B) from which about two fifths the total amount of blood was removed, with little compensation following, a dose of digitalin affected the pulse wave, although it affected the

blood-pressure very slightly, if at all. In a control dog (A) of the same weight, the same dose of digitalin had no appreciable effect. (2) A therapeutic dose of strychnin, which raised the pressure in the normal control dog (A), had no effect on the exsanguinated dog (B). (3) Strychnin in one half tetanic dose, when given to the moribund exsanguinated dog (B), had a lessened symptomatic effect, and an increased effect on the blood-pressure.

EXPERIMENT 43

Morphin; Curare; Hemorrhage

September 2, 1904.

Newfoundland dog; weight, 19 kilos; condition, good. Ether-morphin anesthesia. Other arrangements as in Experiment 1.

2.30.—Control on drum.

2.32.—A dose of 5 c.c. of curare was given subcutaneously.

2.45.—A dose of 3 c.c. of a new solution was given as before.

3.00.—A dose of 2 c.c. of the old solution was given as before.

3.13.—Began to bleed. The respirations were still spontaneous, but were spasmodic. The other muscles were apparently paralyzed. Death occurred from cardiac failure. An attempt at resuscitation was unsuccessful.

EXPERIMENT 44

Morphin; Hemorrhage; Curare

August 8, 1904.

Old yellow mongrel bitch; weight, 6.9 kilos. Ether-morphin anesthesia. Other arrangements as in Experiment 1.

A dose of 5 c.c. of curare was given subcutaneously. Death occurred before a control could be taken. The thyroid gland was very much enlarged.

EXPERIMENT 45

Morphin; Curare; Hemorrhage; Strychnin

August 30, 1904.

Fox terrier dog; weight, 8.1 kilos; condition, good. Ether-morphin anesthesia. Other arrangements as in Experiment 1.

12.24.—Control on drum. Blood-pressure, 170 mm.

12.25.—3.5 c.c. curare were given in the right femoral vein. Artificial respiration was begun after one minute had elapsed.

12.34.—Control. Began to bleed. During the bleeding the effect of the curare wore off, and 1 c.c. more was given.

12.50.—300 c.c. blood removed. Blood-pressure, 34 mm.

12.56.—Blood-pressure, 60 mm. 50 c.c. blood removed (total amount, 350 c.c.). Blood-pressure, 50 mm.

12.58.—A dose of 0.08 mgm. per kilo of strychnin was given in the right femoral vein. The effect was marked. The blood-pressure suddenly rose to 146 mm. after a long latent period, and then sank to 124 mm., where it remained until 1.06.

1.08.—Blood-pressure, 100 mm., and gradually falling.

1.18.—Death occurred.

Summary.—After curare and hemorrhage a double dose of strychnin produced a most marked rise in the blood-pressure, equal to what would have been expected from a tetanic dose, which was maintained for eight minutes, and then gradually fell until death occurred.

EXPERIMENT 46

Morphin; Curare; Hemorrhage; Strychnin; Adrenalin

AUGUST 29, 1904.

Mangy black mongrel bitch; weight, 6.9 kilos; condition, poor. Ether-morphin anesthesia. Other arrangements as in Experiment 1.

3.00.—Control on drum. Blood-pressure, 144 mm. 5 c.c. of curare were given subcutaneously, and 2½ c.c. were given in the left femoral vein. Artificial respiration was begun two minutes afterwards.

3.10.—Control. Blood-pressure, 52 mm.

3.20.—Control. Blood-pressure, 142 mm.

3.22.—Control. Began to bleed.

3.27.—100 c.c. blood removed.

3.30.—125 c.c. blood removed.

3.33.—25 c.c. blood removed (total amount, 250 c.c.). Blood-pressure, 34 mm. There was temporary compensation.

3.43.—0.2 mgm. per kilo of strychnin was given in the right femoral vein. There were no tremors or convulsions. After a latent period of half a minute the blood-pressure rapidly rose to 78 mm., and then there was a slow and steady rise to 100 mm. at 3.53.

3.56.—Control. Blood-pressure, 86 mm., and gradually falling.

4.14.—Blood-pressure, 18 mm. Adrenalin chlorid solution, 200 c.c., 1–50,000, was given in the femoral vein, but with no effect.

Summary.—After curare and hemorrhage a convulsive dose of strychnin produced a marked rise of blood-pressure (58 mm.), which reached the maximum in ten minutes, and which at twenty-one minutes fell below the initial level with rapid cardiac failure. Adrenalin given after the strychnin produced no effect.

EXPERIMENT 47

Morphin; Curare; Hemorrhage; Strychnin; Adrenalin

AUGUST 30, 1904.

Young mongrel bitch; weight, 6.9 kilos; condition, poor. Ether-morphin anesthesia. Other arrangements as in Experiment 1.

12.10.—Control. Blood-pressure, 134 mm.

12.15.—3 c.c. curare were given in the right femoral vein, and artificial respiration was begun one minute afterwards.

12.24.—Began to bleed.

12.29.—200 c.c. blood removed. Blood-pressure, 40 mm.

12.58.—Blood-pressure, 26 mm. $\frac{1}{100}$ grain strychnin (0.09 mgm. per kilo) was given in the right femoral vein. It had no effect.

1.04.—150 c.c. 1–50,000 adrenalin chlorid solution given intravenously had no effect.

Summary.—After giving curare to a dog in poor condition whose heart was rapidly failing before the drugs were given, neither strychnin nor digitalin produced any effect.

POINTS OF SPECIAL INTEREST IN THE PRECEDING PROTOCOLS

Hemorrhage.

1. During a very rapid hemorrhage the blood-pressure continued to fall for some time before compensation began.—*Experiment* 20.

2. With an even rate and a rapid hemorrhage the blood-pressure fell unevenly. The greatest fall occurred just after or toward the end of the loss of the first third of the blood removed.—*Experiments* 3, 25, 26, 28, 29.

3. With a slow hemorrhage the rate of fall of blood-pressure was more uniform.—*Experiment* 27.

4. In death from hemorrhage the respiratory center failed first.—*Experiments* 2, 9.

5. After hemorrhage, a diminished vasomotor reflex was associated with falling of the blood-pressure until death occurred.—*Experiment* 14.

6. After hemorrhage, manipulation of the larynx produced respiratory inhibition, but no further fall of the blood-pressure. —*Experiment* 4.

7. After a hemorrhage of about 0.6 of the total amount of blood, spontaneous compensation may bring the blood-pressure back to a level at which life may be maintained.—*Exp.* 11.

8. (*a*) After hemorrhage, good compensation was associated with active vasomotor centers.—*Experiments* 12, 16, 22, 33, 35.

(*b*) After hemorrhage, failure of compensation was associated with loss of activity of the vasomotor centers, and poor compensation was associated with feeble reaction.—*Experiments* 10, 13, 14, 16, 30, 32, 33, 40.

Normal Saline Infusion.

1. After a long delay after hemorrhage the rapid infusion of normal saline solution had little if any favorable effect on the blood-pressure. It was followed by respiratory failure, and cardiac dilatation.—*Experiment* 4.

2. A rapid saline infusion shortly after hemorrhage did not maintain the blood-pressure at the level to which it raised it.—*Experiments* 8, 23, 24.

3. After hemorrhage, a rapid saline infusion (100 c.c. in two or three minutes) overtaxed the heart without necessarily disabling it.—*Experiments* 16, 23, 24, 30, 40.

4. After a long delay after hemorrhage, the infusion of saline solution at a moderate rate raised and maintained the blood-pressure but a short time.—*Experiment* 16.

5. After a long delay after hemorrhage, when compensation had failed and the vasomotor centers had failed to react to stimulation, saline infusion affected the blood-pressure but slightly, if at all.—*Experiment* 13.

6. After a long delay after hemorrhage, saline infusion in very moderate amount, and given at a moderate rate when compensation had failed, caused transudation into the splanchnic area.—*Experiment* 13.

7. After infusing an amount of saline solution equal to the amount of blood withdrawn during hemorrhage, a further infusion was associated with lowering of the blood-pressure, even if the heart was not overtaxed.—*Experiments* 31, 34.

8. An infusion of saline solution in amount in excess of the amount of blood removed during hemorrhage markedly embarrassed the respiration.—*Experiments* 8, 23.

9. When saline infusion with a little adrenalin was given rapidly in cardiac failure from hemorrhage, the heart was revived, but usually complete failure soon followed.—*Experiment* 15.

10. After a short wait after hemorrhage followed by complete failure of compensation, properly given saline infusion affected the blood-pressure but little, or not at all, and did not promote recovery.—*Experiments* 11, 22.

11. After a long wait after hemorrhage, but with compensation well sustained, saline infusion was effective in further raising the blood-pressure.—*Experiment* 11, *Dog B*.

12. After hemorrhage saline infusion given at once, at first rapidly, then slowly, possibly raised the blood-pressure well up toward the normal level.—*Experiment* 5.

13. After a long wait after hemorrhage, saline infusion caused but little rise in the blood-pressure after a certain limit had been reached, and the rapid infusion of enough more to equal the amount of blood lost embarrassed the respiration and

circulation, while a slower rate was well borne, and, if very slow, brought the animal to a normal condition, although with a low blood-pressure.—*Experiments* 10, 38.

14. When no compensation had appeared after a considerable time had elapsed after hemorrhage, normal saline infusion had a much diminished effect.—*Experiment* 38.

15. After a long delay after hemorrhage, normal saline infusion brought back the activity of the vasomotor centers but slightly, or not at all.—*Experiments* 5, 13, 37.

16. When given a short time after hemorrhage, normal saline infusion brought back the activity of the vasomotor centers well.—*Experiments* 16, 24, 29, 30, 31.

17. After exhaustion of the vasomotor centers and heart from hemorrhage and from strychnin in convulsive dose, or from hemorrhage alone, normal saline infusion was not effective.—*Experiments* 27, 28.

18. After hemorrhage, a long wait, and a therapeutic dose of strychnin, normal saline infusion had no effect.—*Experiment* 28.

19. After hemorrhage and strychnin-induced compensation, normal saline infusion had a temporary and diminished effect.—*Experiment* 26.

20. When given at a moderately short time after hemorrhage (twenty to thirty minutes), rapid saline infusion brought back the blood-pressure halfway to the original level, but cardiac failure soon followed.—*Experiment* 25.

21. Marked compensation after hemorrhage, if not sustained by saline infusion, was quickly followed by respiratory and cardiac failure.—*Experiments* 12, 22.

22. After hemorrhage and normal saline infusion, the close application of a rubber bandage to the extremities and abdomen raised the blood-pressure to a decidedly and uniformly higher level.—*Experiment* 29.

23. After hemorrhage, the immediate infusion of Locke's solution at a moderate rate brought the blood-pressure back nearly to the original level. (The vasomotor centers seemed to be active, although not fully so, in Experiment 32, and showed a moderate effort at producing compensation in Experiment 31.)—*Experiments* 31, 32.

24. After a long wait after hemorrhage, the infusion of Locke's solution at a moderate rate raised the blood-pressure well, but did not maintain it, and caused respiratory and cardiac failure.—*Experiment* 33.

25. After hemorrhage, the infusion of Locke's solution, although given immediately at a slow rate, brought back the blood-pressure poorly, and only temporarily.—*Experiment* 34.

Strychnin.

1. After hemorrhage and recovery by means of normal saline infusion, strychnin in therapeutic dose did not increase the activity of the vasomotor centers.—*Experiment* 31.

2. After hemorrhage and recovery by means of normal saline infusion, a triple therapeutic dose of strychnin did not increase the activity of the vasomotor centers, although it might have raised the level of the blood-pressure.—*Experiments* 31, 40.

3. After hemorrhage, strychnin did not increase the activity of the vasomotor centers.—*Experiment* 35.

4. After hemorrhage followed by failure of compensation, strychnin in therapeutic dose did not assist normal saline infusion in restoring the normal functions.—*Experiment* 22.

5. A therapeutic dose of strychnin had more effect on control dogs than on dogs which underwent hemorrhage.

6. In moribund, exsanguinated dogs strychnin had a lessened symptomatic effect, and an increased effect on the blood-pressure.

7. After hemorrhage, overdoses, subtetanic, and tetanic doses of strychnin affected the blood-pressure relatively less than the pulse wave, or not at all, and were followed by violent overaction of the heart, and sometimes followed by rapid cardiac failure.—*Experiments* 17, 18, 19, 20, 27.

8. After hemorrhage, a double therapeutic dose of strychnin was followed by overaction of the heart (which sometimes recovered) and respiratory failure.—*Experiments* 26, 35.

9. After hemorrhage, the latent period for the action of strychnin was increased (ether anesthesia).—*Experiments* 19, 20.

10. Immediately after hemorrhage, a double therapeutic dose of strychnin was followed by more than the usual effect. —*Experiment* 26.

11. After hemorrhage, a double therapeutic dose of strychnin was not followed by any effect on the blood-pressure.—*Experiments* 27, 28, 37.

12. After hemorrhage with subsequent overaction of the vasomotor centers due to strychnin, a further dose of strychnin, up to an almost tetanic amount, caused no rise in the blood-pressure.—*Experiment* 26.

13. After hemorrhage and the administration of an infusion of either normal saline solution or Locke's solution, strychnin in therapeutic dose, given either before or after the infusion, did not affect the blood-pressure.—*Experiments* 25, 31, 40.

14. After hemorrhage and subsequent partial recovery by means of normal saline infusion, strychnin in tetanic dose caused a marked rise of blood-pressure which was at once followed by cardiac failure.—*Experiment* 24.

15. After hemorrhage and subsequent partial recovery by means of normal saline infusion an overdose of strychnin caused the characteristic reaction.—*Experiment* 23.

16. After curare and hemorrhage, a tetanic or large therapeutic dose of strychnin caused a marked rise of blood-pressure which was followed by rapid cardiac failure.—*Experiments* 45, 46.

17. After hemorrhage, and recovery by means of normal saline infusion with a subsequent falling blood-pressure, strychnin in tetanic dose had no effect.—*Experiment* 34.

18. After hemorrhage and normal saline infusion, a double therapeutic dose of strychnin did not cause a rise in the blood-pressure.—*Experiment* 29.

19. After hemorrhage and normal saline infusion, a therapeutic dose of strychnin caused only a temporary rise of blood-pressure.—*Experiments* 30, 32.

Digitalin.

1. Digitalin affected the pulse wave of a bled dog more than it affected the pulse wave of a control dog.—*Experiments* 41, 42.

2. After hemorrhage digitalin had a deleterious effect, and hastened death.—*Experiments* 35, 38, 39.

Adrenalin.

1. After hemorrhage adrenalin raised the mean blood-pressure relatively less than it does under normal circumstances, and brought on rapid cardiac failure.—*Experiments* 16, 36, 37.

DISCUSSION AND CONCLUSIONS

In all varieties of hemorrhage from normal animals there is an immediate tendency to a compensatory or natural recovery. Granting the truth of this statement, the question at once arises as to just what a "compensatory recovery" is. In other

words, what do we mean when we say that "compensation" occurs in the course of a hemorrhage?

Compensation may be defined as being the natural effort of the circulatory system to maintain a normal or at least efficient blood-pressure after diminution of the efficient vascular content. The phrase "efficient vascular content" is used advisedly for the reason that compensation occurs in shock as well as in hemorrhage, and while in shock the total vascular content is not decreased by loss from the vessels, part of it is rendered inefficient by reason of stasis in the vascular trunks.[1]

Roughly speaking, compensation is noted in all the grades of hemorrhage until such a degree has been reached that the vasomotor center is no longer actively responsive to reflex stimulation, such as burning a paw or stimulating the sciatic nerve. With the hemorrhage and the fall in the blood-pressure the specific gravity of the blood falls. After the hemorrhage has proceeded until there is no effort at compensation the animal unaided rarely recovers. If the blood-pressure is raised either by saline infusion, by bandaging, or by the administration of adrenalin, sometimes the centers become more active, and the blood-pressure assumes and holds a higher level.

In experiments in which the hemorrhage was continued until there was no spontaneous compensation, and there was no response to reflex stimulation, the animal could rarely be made to recover. There was a marked difference in the final result if an interval intervened between the time of the ending of the hemorrhage and the beginning of treatment. *The longer the interval of low blood-pressure the less marked were the effects of treatment.* In rapid bleeding the blood-pressure continues to fall after the cessation of the hemor-

[1] The reader is referred to "Blood Pressure in Surgery" and to "Surgical Shock," Crile.

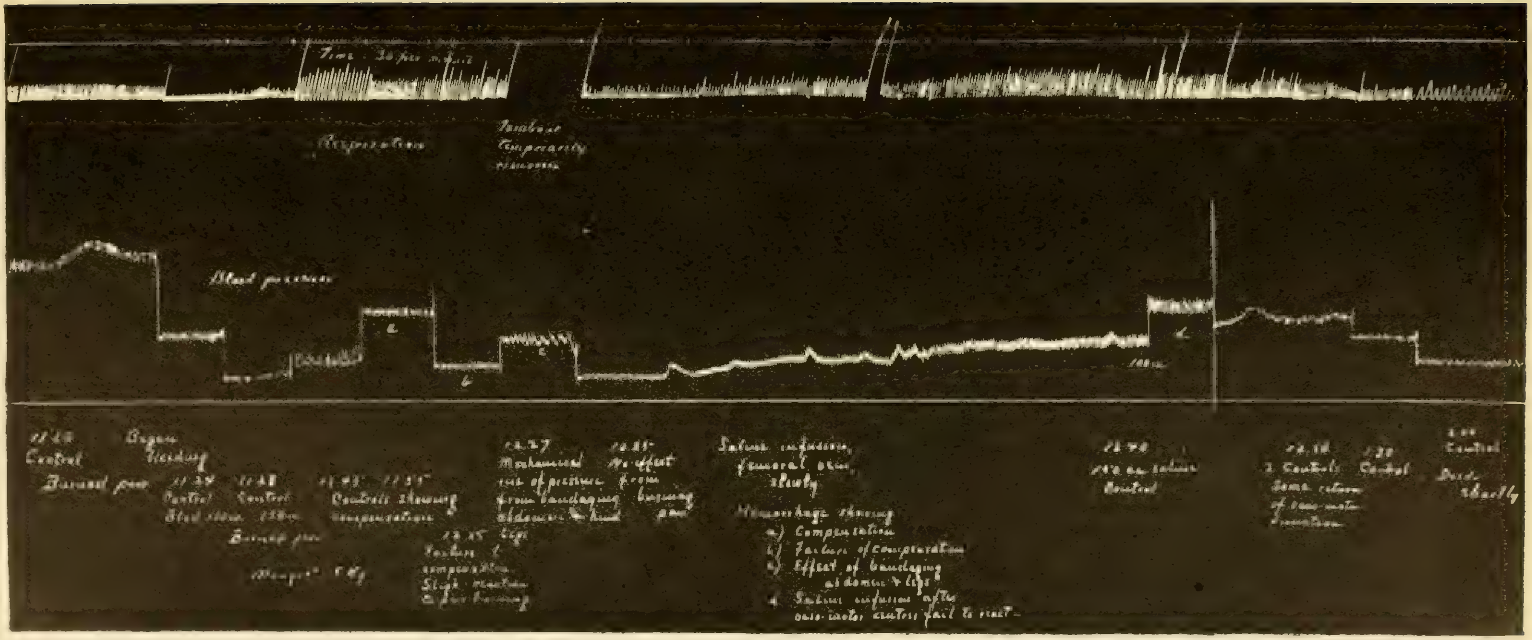


FIG. 1.—(*a*) Compensation after profound hemorrhage (rise of 50 mm. Hg.). (*b*) Failure of compensation, associated with diminished reaction of the vasomotor centers to peripheral stimulation. (*c*) Blood-pressure raised mechanically by bandaging abdomen and extremities (rise of 22 mm.). (*d*) Intravenous infusion of saline solution, after almost complete failure of the vasomotor centers, reactivated them only partly and temporarily.

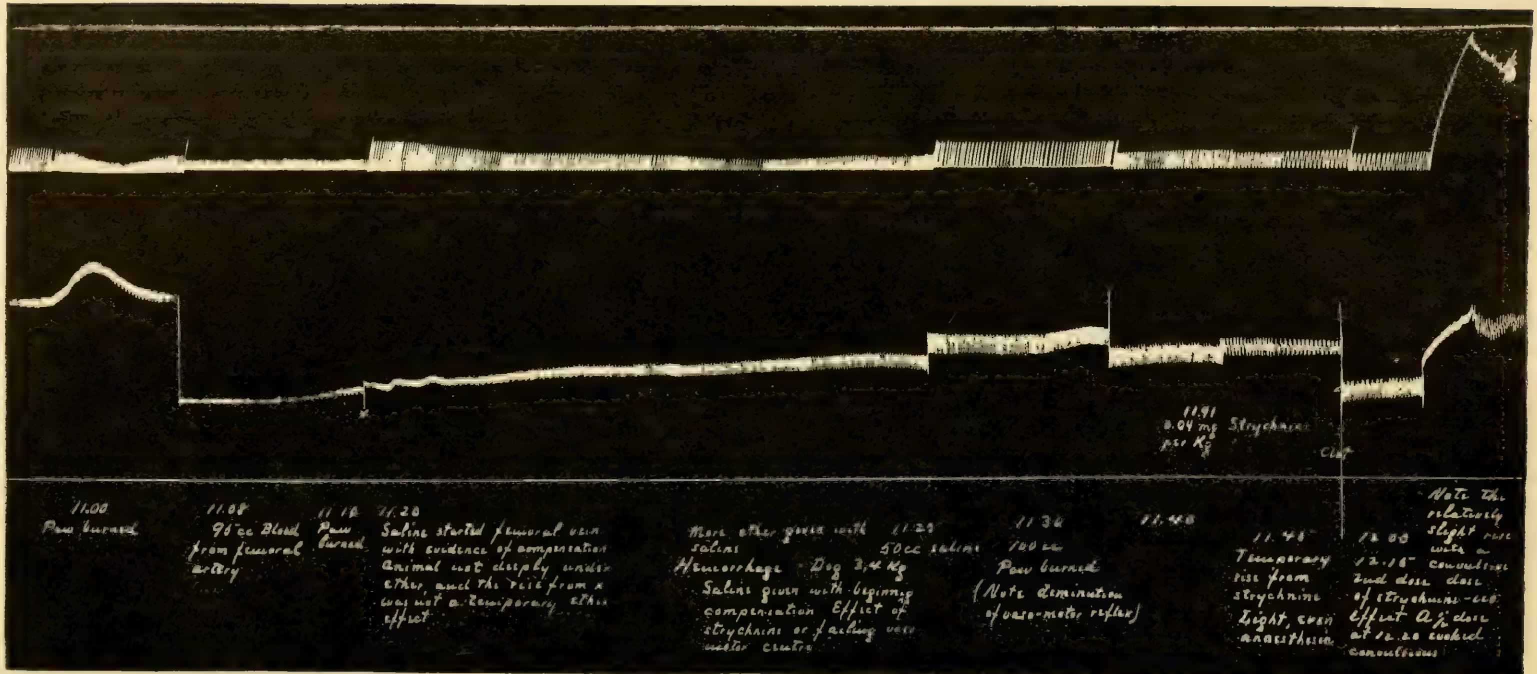


FIG. 2.—INTRAVENOUS INFUSION OF SALINE SOLUTION AFTER HEMORRHAGE, STARTED BEFORE COMPLETE FAILURE OF THE VASOMOTOR CENTERS, ONLY PARTIALLY REACTIVATED THEM, AND THE BLOOD-PRESSURE QUICKLY FELL FROM THE MAXIMUM LEVEL REACHED. Strychnin in therapeutic dose, given at the beginning of the decline, raised the blood-pressure temporarily 7 mm. Hg., but after one half hour, after a further fall of blood-pressure, associated with a progressive diminution of the reaction of the vasomotor centers to peripheral stimulation (not shown on the tracing), a second dose of strychnin had no effect, and while a third dose evoked convulsions, the rise of pressure was relatively small. (The upper tracing is respiration, the lower, blood-pressure. Time in seconds.)

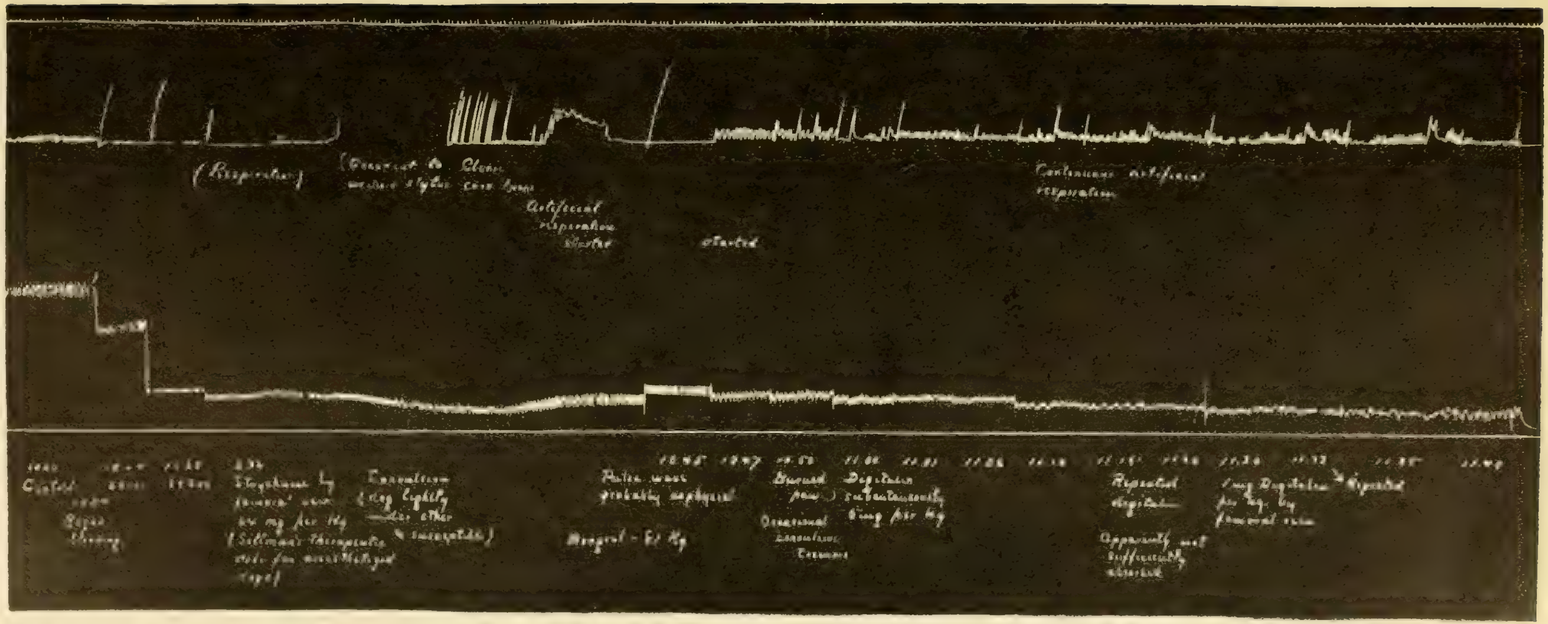


FIG. 3.—THE EFFECT OF DRUGS AFTER HEMORRHAGE, THE VASOMOTOR CENTERS NOT REACTING TO PERIPHERAL STIMULATION (10.32 CONTROL, *q.v.*). (*a*) Strychnin in the usual therapeutic dose for anesthetized dogs unexpectedly caused convulsions, but even with this reaction there was no rise in blood-pressure. (*b*) Digitalin was apparently not absorbed when given subcutaneously, but a moderate intravenous dose (2 mgm. per kilo) caused rapid cardiac failure.

6

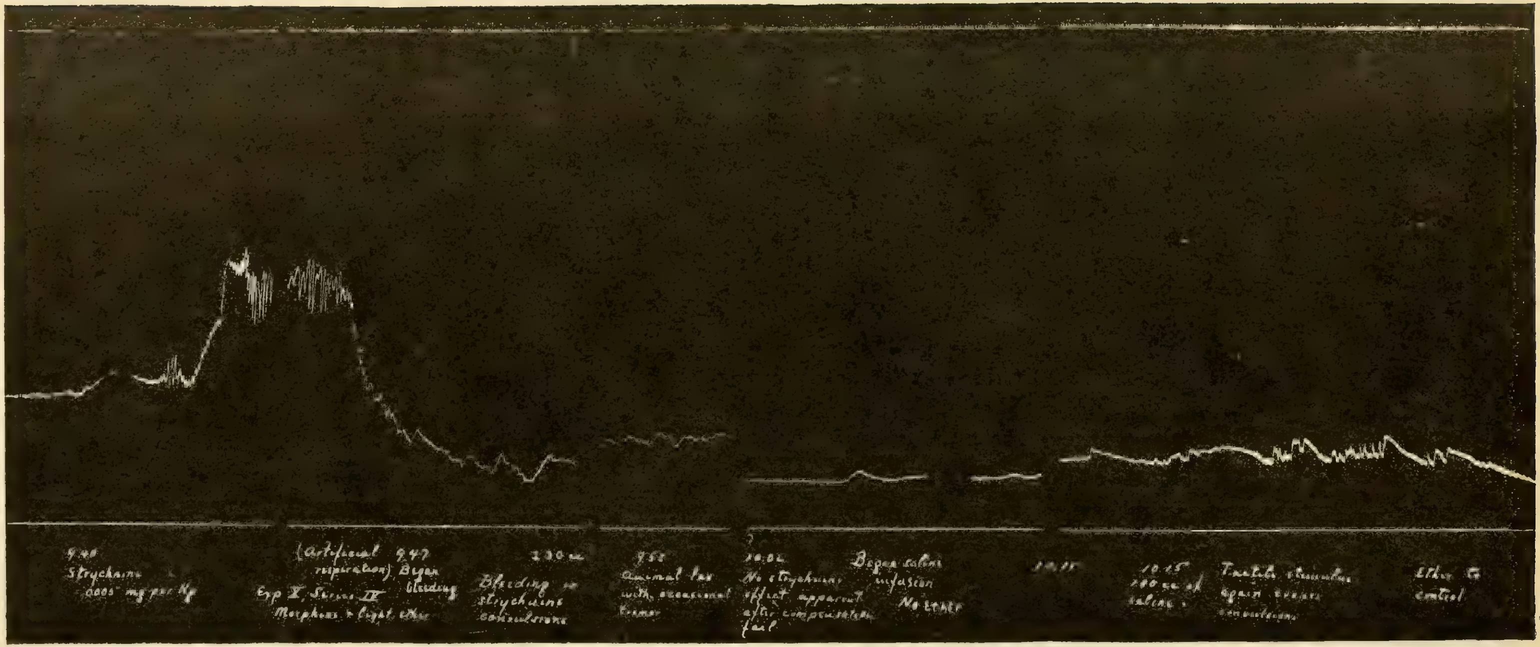


FIG. 4.—CONVULSIONS CAUSED BY A SLIGHT OVERDOSE OF STRYCHNIN WERE COMPLETELY CONTROLLED BY RAPID BLEEDING TO A LEVEL OF 36 MM. HG. WITHOUT ETHER (THE DOG WAS UNDER THE INFLUENCE OF MORPHIN). When the blood-pressure was raised to 56 mm. (the initial level was 100 mm.) by means of saline infusion, the convulsions recurred.

rhage. The extent of the recovery depends upon the individuality of the animal and amount of the hemorrhage. The proportion of lost blood to the body weight that animals withstood and recovered from varied considerably in individual cases. This degree of variation seemed to us to be greater than is usually given. In some animals recovery occurred when three fifths of the estimated blood had been lost, while in others death would occur after a loss of two fifths. It was impossible to estimate in any given animal with any degree of accuracy the proportion of blood to its body weight which it might lose and recover.

What, then, are the secondary factors entering into the fall in the blood-pressure and its recovery? It may be assumed that the primary factor is anemia with consequent lessening of the immediate nutrition of the active physiological mechanism for the maintenance of the normal blood-pressure.

Among the secondary factors we may assume that the action of the vasomotor center [1] stands first. Exomosis from the tissues is also an important factor. That the vasomotor center is the most important secondary factor is shown by the following:

1. When an animal was bled very considerably, even to a dangerous degree, and there was still some natural compensation, though amounting to only a few millimeters of mercury, and this animal was then given a therapeutic dose of strychnin, the blood-pressure usually rose considerably over a short period of time. Since this rise in the blood-pressure as a result of the physiological dose of strychnin is known to be due to a stimulation of the vasomotor center, we may then conclude that could the vasomotor center have a spontaneous

[1] Whether the synapse or the cell as a whole is responsible the author expresses no opinion, but the phrase "vasomotor center" is throughout these pages meant to include the central nerve mechanism in contradistinction to the conducting paths.

stimulation, or an automatic stimulation equal to that of strychnin, and should this stimulation of this center be continued, the animal would make a prompt and effective recovery from such degree of hemorrhage. On the other hand, if no strychnin is given in such a case, the blood-pressure is likely to remain at or near the level of the first compensation, and after a period of time and inversely with the lapse of time, the effect of a later stimulation is less marked. It would seem that the vasomotor center becomes less active as the anemia is continued.

2. In animals in which the vasomotor center has been previously impaired by shock, the compensation after hemorrhage is less marked, and its response to vasomotor stimulations likewise less.

3. In animals in which the functional activity of all the centers is greatly reduced by reason of malnutrition or disease compensation is less marked.

4. The heart itself is unable to affect the blood-pressure materially because it has been shown that the rate and force of the contraction of the heart has, under any and all circumstances, but limited power of raising the blood-pressure.

It may, too, add to the support of the importance of the vasomotor factor to note that if a large dose of adrenalin is added to the circulation even after death, and the action of the heart is substituted by manual pressure, the blood-pressure still may rise. That is to say, the question of compensation (hence recovery after hemorrhage) is very largely one of dynamics, and concerns primarily the vasomotor center. Since it is noted that the addition of any fluid to the circulation in the lower though not the lowest states of blood-pressure causes a rise in the pressure, we must grant that the addition of fluid from the extravascular tissues of the animal itself must, on the grounds of analogy, play its part, though it be a minor one.

The specific gravity of the blood, the hemoglobin determination, and the red blood count all show very marked variations in the different experiments and in various parts of the same experiment. The first effect noted upon the respiration in the primary arterial hemorrhage is an increase in rate.

TREATMENT

The Effects of Certain Drugs

The effect of drugs varies in the different parts of the circulatory apparatus in the various degrees of arterial hemorrhage. They not only showed these distinctions, but also presented a marked difference in their effects in the various periods of time after the hemorrhage at which they were administered.

Strychnin.—The effect of strychnin when immediately given in the various degrees of arterial hemorrhage diminished as the hemorrhage increased. After a slight hemorrhage the blood-pressure was raised almost as much as in the control dog. In profound hemorrhage in a few instances no effect on the blood-pressure was noted. When the therapeutic doses of strychnin were repeated in the cases in which there was a distinct effect upon the blood-pressure, the effect of the second dose was usually less marked than that of the first, and sometimes no effect whatever was noted. However, in all the instances of profound hemorrhage the longer the interval between the hemorrhage and the administration of strychnin, generally speaking the less marked was the effect of strychnin on the blood-pressure. If, however, there were still left some compensatory power in a profound hemorrhage, and the *blood-pressure was first raised as much as possible by saline infusion, the effect of strychnin was then more marked.*

The effect of strychnin on the heart itself was more marked in the cases of deep hemorrhage than on the control dogs. Its apparent effect on the heart in any of the experiments, excepting those in which a large hemorrhage had been produced, was not marked.

Digitalis.—What has been said as to the effect of strychnin on the vasomotor center may be said of digitalis, although in the case of digitalis there was markedly greater uncertainty and irregularity in the results.

The effect of digitalis on the heart showed a more distinct difference. The deeper the hemorrhage and the lower the blood-pressure, the more marked were the effects on the heart; these effects being an alteration in the rhythm and the frequency of the heart beats and in many cases sudden cardiac failure. The action on the heart was more constant than the action on the vasomotor center.

Oxygen.—The favorable effect of oxygen inhalation during the critical stages of hemorrhage was in almost every instance well marked.

Saline Infusion.—In the vast majority of experiments saline infusion was followed by an immediate rise in the blood-pressure, with an increase in the pulse volume and the output of the heart. In the experiments in which the blood-pressure was reduced so low that no spontaneous compensation was noted, occasionally it was found that there was no rise in the mean blood-pressure on administering saline solution. The increase in the output of the heart and in the pulse volume at the same time was markedly increased. In the majority of instances in the various degrees of less profound hemorrhage, the principal effect of saline solution was that of raising the blood-pressure. In the cases in which the saline solution was given rapidly, the highest point first obtained was usually not maintained. In some instances the blood-pressure would con-

tinue to rise after the cessation of the saline solution, and the general condition of the animal was markedly improved, but in other instances, especially those in which hemorrhage was profound, the saline infusion caused extreme embarrassment of the heart action, even a fatal dilatation. We may then consider the effect of the saline infusion as follows: (1) Its effect on the vasomotor center; (2) its effect on the heart.

1. *The Vasomotor Center.*—For the most part, the vasomotor centers seem to be favorably influenced by the increased blood-pressure and increased circulation established by the infusion. There were instances in which, even though there was no increase in the blood-pressure, it at least held its own at a higher level; then, again, it was sometimes noted that after a rise in blood-pressure, burning a paw elicited a greater activity of the vasomotor center than was noted before. In these cases, too, the administration of strychnin caused a more marked effect on the vasomotor center. That is to say, it seemed that the increased circulation through the vasomotor center by means of the saline infusion increased the activity of this center. There were no cases in which it was clearly observed that saline infusion affected the vasomotor center especially unfavorably.

2. *The Heart.*—While in the case of the vasomotor center the effect of saline solution was either to increase its activity, or at least not to damage it, in the case of the heart the same results were not always noted. In certain instances, especially when the infusion was given rapidly, and the heart was very anemic, an acute, sometimes fatal, dilatation was noted. Many times the heart was greatly embarrassed, though it finally recovered. It is well here to call attention to the fact that the work of the heart when the volume of fluid is augmented is increased in a geometric ratio. That is to say, if twice the amount of fluid is suddenly thrown into the heart its work is

not doubled, but quadrupled. It was found more effective to give a guarded infusion at first, noting the effect on the heart, then gradually increasing it as the heart itself became able to assume more work. Substitution of oxygenated Locke's solution or Ringer's solution for normal saline apparently gave better results.

Other Comments.—When the saline infusion was given continuously in rather too large amount, it was rapidly transferred to the splanchnic area, escaping through the vessels, and filling the walls and lumena of the hollow viscera. The effect, then, of saline solution is limited to the influence it may have in its transit through the circulatory apparatus. The effect in respect to the heart and the vasomotor center, as in the case of strychnin and digitalis, depended somewhat on the length of time that elapsed before the ending of the hemorrhage and the beginning of the infusion. The later the infusion, the less favorable was the effect. Saline infusion, though a valuable agent, has strict limitations. It is at best a poor substitute for blood.

Bandaging the extremities and trunk raised the pressure and maintained it, although the rise was not large, and no unfavorable effects were noted.

Note.—The treatment of hemorrhage by transfusion is taken up fully in Part II, and is, therefore, not considered here.

CHAPTER II

THE COMPARISON OF THE EFFECTS OF ACUTE HEMORRHAGE AND OF SHOCK ON THE BLOOD MASS

In collaboration with Drs. F. W. Hitchings, C. H. Lenhart, and A. S. Eisenbrey.

In order to determine the number of red and of white corpuscles, and the amount of hemoglobin, both before and after subjecting dogs to hemorrhage and to shock, respectively, four experiments were undertaken with the hope that they would at least serve as a basis for later work, even if they were not sufficiently conclusive in themselves. In each experiment two dogs of as nearly the same size as could be obtained were anesthetized with ether. A carotid artery of each animal was exposed and connections with a manometer and the same smoked drum were established. The number of white and of red corpuscles of each was determined by means of a Thoma-Zeiss blood counter, and the hemoglobin was estimated by means of the Tallqvist hemoglobin scale. Then one dog was bled at irregular intervals from a femoral artery, while the other was reduced to shock by various means, the endeavor being to reduce the blood-pressure equally and simultaneously as shown by controls taken on the drum. As the experiment progressed the blood counts and hemoglobin determinations were made at intervals of about one hour. On one day the examinations of the blood of the shock dog were carried through by an observer who took the hemorrhage dog the next day, in order to prevent as far as possible any individual factors from detracting from the accuracy of the results. The blood for the

examinations was taken from the peripheral circulation, usually by pricking the tip of the nose.

In the hemorrhage dogs it was found in all the experiments that there was a marked increase in the rapidity of the coagulation of the blood, and that the more the dog was bled the more difficult it was to obtain blood from the peripheral circulation. No attempt was made to examine blood from a central vein or artery, as in doing so a departure would have been made from the method that would ordinarily be employed clinically. No attempt was made to determine the relative time of coagulation in the two conditions, but it was very evident that the blood of the shock dogs at least did not have the coagulation time shortened, and it did not seem to be lengthened, judging from the observations of the blood collected for examination.

PROTOCOLS OF EXPERIMENTS

EXPERIMENT 1

Shock Dog.—Yellow mongrel bitch with slightly enlarged thyroid gland; weight, 9 kilos; condition, fair. *Hemorrhage Dog.*—White mongrel dog; weight, 7.7 kilos; condition, good.

Time	Control (for both dogs)	Shock Dog		Hemorrhage Dog	
			Blood-Pressure		Blood-Pressure
10.14	1.	Blood count (1).	110 mm. Hg.	Blood count (1).	105 mm. Hg.
10.27	2.	Began shock.	74 " "	Began bleeding from femoral artery.	82 " "
10.50	3.	Stopped shock.	64 " "	Stopped bleeding. 200 c.c. removed.	88 " "
11.20	4.	Blood count (2).	62 " "	Blood count (2).	82 " "
11.50	5.		60 " "		79 " "
12.20	6.	Blood count (3).	60 " "	Blood count (3).	34 " "
12.51		Dog killed.		Death occurred suddenly with the right heart paralyzed in diastole (due primarily to the ether).	

THE BLOOD COUNTS

No.	Shock Dog			Hemorrhage Dog		
	Red Cells	Hemo-globin	White Cells	Red Cells	Hemoglobin	White Cells
1	7,500,000	100%	8,000	7,856,000	98%	6,000
2	6,400,000	100%	16,000	5,888,000	90%	8,000
3	7,660,000	98%	11,500	7,160,000	85%	18,200

EXPERIMENT 2

Shock Dog.—Fat black mongrel bitch; weight, 12.2 kilos; condition, good. *Hemorrhage Dog.*—White mongrel dog; weight, 11.4 kilos; condition, good.

Time	Control (for both dogs)	Shock Dog		Hemorrhage Dog	
			Blood-Pressure		Blood-Pressure
9.30	1.	Blood count (1).	114 mm. Hg.	Blood count (1). Rapid bleeding from carotid artery which began by accidental slipping of cannula. 180 c.c. removed.	128 mm. Hg.
9.40	2.	Shock begun.	111 " "		128 " "
10.15	3.	Blood count (2).	105 " "	Blood count (2). Bled 170 c.c. slowly.	33 " "
10.40	4.	Blood count (3).	92 " "	Blood count (3).	87 " "
10.50		More shock.			
11.00	5.		82 " "		81 " "
11.10				Bled 50 c.c. Total amount blood removed 400 c.c.	
11.30	6.	Blood count (4).	88 " "	Blood count (4).	79 " "
11.35		Death from magnesium sulphate solution in manometer getting into the circulation.		Respiration stopped for 2 minutes. Artificial respiration used.	
12.00	7.			Bled 100 c.c. slowly. Total amount of blood removed 500 c.c.	6 " "
12.30	8.			Dog killed.	10 " "

THE BLOOD COUNTS

No.	Shock Dog			Hemorrhage Dog		
	Red Cells	Hemo-globin	White Cells	Red Cells	Hemoglobin	White Cells
1	8,440,000	100%	23,800	6,440,000	100%	16,000
2	8,304,000	100%	12,400	5,832,000	90%	11,500
3	8,944,000	100%	9,100	6,248,000	80%	23,000
4	8,933,000	100%	8,200	4,792,000	75%	19,200

EXPERIMENT 3

Shock Dog.—Brown, smooth-coated bitch; weight, 9.9 kilos; condition, good. *Hemorrhage Dog.*—Brown, smooth-coated bitch; weight, 8.1 kilos; condition, good.

Time	Control (for both dogs)	Shock Dog		Hemorrhage Dog	
			Blood-Pressure		Blood-Pressure
9.45	1.	Blood count (1).	144 mm. Hg.		148 mm. Hg.
9.50		Shock begun.		Blood count (1).	
10.10	2.		144 " "	Began to bleed slowly.	158 " "
10.35		Rectal temperature 37.0° C.		Stopped bleeding. 200 c.c. removed. Temp. 37.0° C.	
10.36	3.		70 " "		120 " "
10.50	4.	Temp. 36.0° C.	91 " "	Temp. 37.0° C.	130 " "
		Blood count (2).		Blood count (2).	120 " "
11.10	5.	More shock.	97 " "	Began to bleed.	120 " "
11.21	6.	Temp. 36.0° C.	32 " "	Stopped bleeding. 100 c.c. removed. Temp. 36.0° C.	98 " "
11.50	7.	Blood count (3).	40 " "	Blood count (3).	100 " "
12.15		More shock.			
12.35	8.	Temp. 35.0° C.	72 " "	Temp. 35.5° C.	104 " "
12.42		Death from magnesium sulphate solution flowing into vessels from manometer.			
12.50	9.			Blood count (4).	52 " "
1.19	10.			Began to bleed.	58 " "
1.26	11.			Stopped bleeding. 50 c.c. removed. Total 350 c.c.	52 " "
1.30	12.			Blood count (5). Temp. 35.0° C. Dog killed.	42 " "

THE BLOOD COUNTS

No.	Shock Dog			Hemorrhage Dog		
	Red Cells	Hemoglobin	White Cells	Red Cells	Hemoglobin	White Cells
1	6,184,000	100%	25,000	5,480,000	100%	21,000
2	6,608,000	100%	6,900	5,128,000	100%	4,600
3	6,968,000	100%	6,400	5,088,000	80%	17,000
4				5,664,000	75%	10,200
5				5,760,000	77%	22,400

EXPERIMENT 4

Shock Dog.—Black mongrel dog; weight, 9 kilos; condition, good. *Hemorrhage Dog.*—Black and tan mongrel dog; weight, 14.4 kilos; condition, good.

Time	Control (for both dogs)	Shock Dog		Hemorrhage Dog	
			Blood-Pressure		Blood-Pressure
9.55	1.	Blood count (1).	128 mm. Hg.	Blood count (1).	126 mm. Hg.
10.15	2.		140 " "		102 " "
10.18		Began shock.		Began to bleed.	
10.30	3.	Temp. 37.0° C.	114 " "	Temp. 37.0° C. Stopped bleeding. 200 c.c. removed.	85 " "
10.40	4.		85 " "	125 c.c. bled.	58 " "
10.55	5.	Blood count (2). Temp. 38.0° C.	92 " "	Blood count (2). Temp. 38.0° C.	75 " "
11.05		More shock.		Began to bleed.	
11.16	6.	Temp. 37.0° C.	80 " "	Temp. 38.0° C. Stopped bleeding. 125 c.c. removed.	65 " "
11.35	7.	More shock.	76 " "	Began to bleed.	76 " "
11.44				Stopped bleeding. 100 c.c. removed. Total am't removed 550 c.c.	
11.56	8.	Temp. 37.0° C. Blood count (3)	56 " "	Temp. 38.0° C. Blood count (3).	70 " "
12.15	9.		60 " "		54 " "
12.55	10.	Blood count (4). Temp. 38.0° C. There was some oozing of serum from the peritoneum.	84 " "	Blood count (4). Temp. 38.0° C.	76 " "
			76 " "		72 " "
1.30	11.		80 " "	Blood count (5).	58 " "
1.55	12.				

THE BLOOD COUNTS

No.	Shock Dog			Hemorrhage Dog		
	Red Cells	Hemoglobin	White Cells	Red Cells.	Hemoglobin	White Cells
1	5,920,000	100%	23,600	8,288,000	100%	7,500
2	6,240,000	100%	10,400	7,872,000	80%	5,200
3	5,216,000	100%	14,000	8,576,000	77%	4,100
4	7,200,000	100%	25,000	7,784,000	85%	11,500
5				7,520,000	80%	26,000

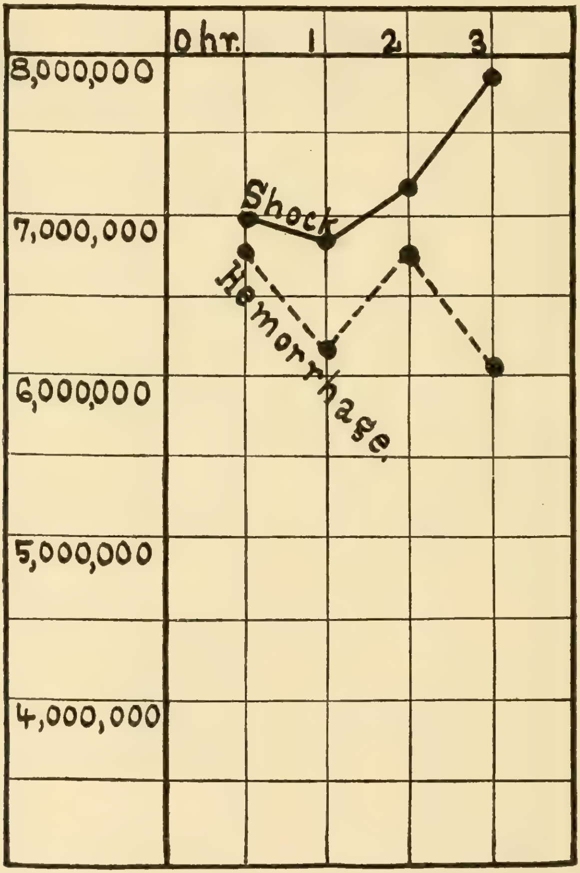


FIG. 5.—COMPARISON OF THE EFFECTS OF HEMORRHAGE AND OF SHOCK ON THE BLOOD OF DOGS. The Red Corpuscles.

SUMMARY OF EXPERIMENTAL FINDINGS

A study of the curves derived from averaging the figures of all the experiments shows the following results (the curves represent *approximate* values only):

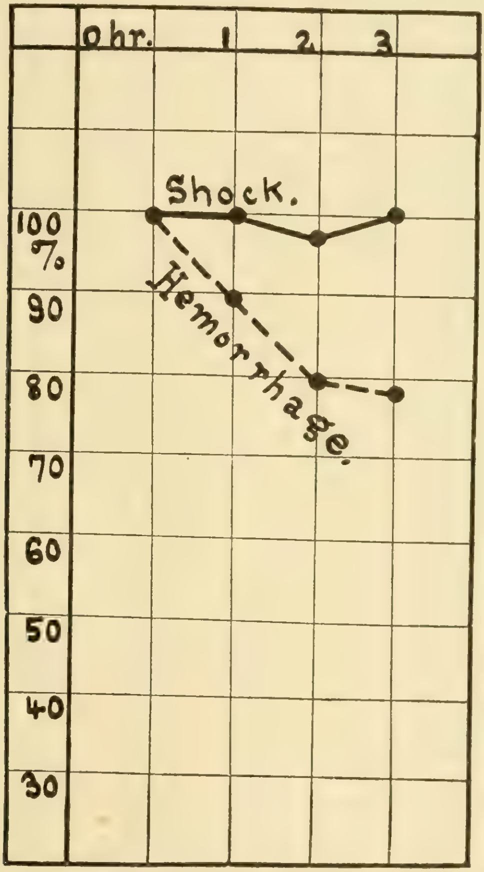


FIG. 6.—COMPARISON OF THE EFFECTS OF HEMORRHAGE AND OF SHOCK ON THE BLOOD OF DOGS. The Hemoglobin.

NOTE.—In Figs. 5, 6, and 7 the curves are based on *approximate* averages derived from four experiments only. They are inserted merely to give a general impression of the changes which may occur.

1. In the blood of the shock dogs there was an increase in the number of the red cells per cubic millimeter (a relative increase), while in the blood of the hemorrhage dogs there was

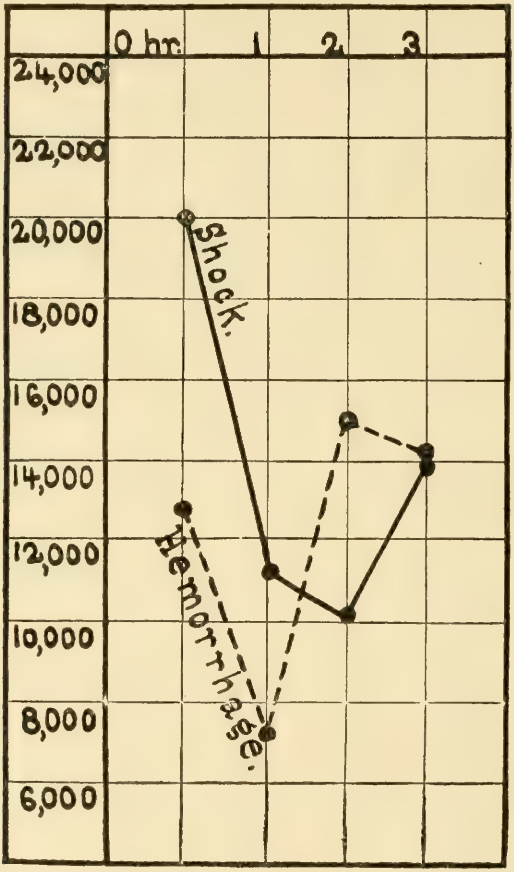


FIG. 7.—COMPARISON OF THE EFFECTS OF HEMORRHAGE AND OF SHOCK ON THE BLOOD OF DOGS. The White Corpuscles.

a decrease in the number of red cells per cubic millimeter (an actual decrease).

2. In the shock dogs there was practically no change in the amount of hemoglobin that could be determined by the

Tallqvist method—at least the amount was not decreased. In the hemorrhage dogs the hemoglobin was reduced in rough ratio to the loss in the red cells (an actual decrease).

3. In the shock dogs there was a decrease in the number of white corpuscles (a relative decrease), while in the hemorrhage dogs there was a preliminary decrease (an actual decrease?) followed by a marked increase (a relative increase).

In presenting these results it is fully realized that they are derived from but few experiments, but, as will be shown, the clinical observations on acute hemorrhage have confirmed the hemorrhage findings in almost every detail.

CLINICAL STUDIES

CHAPTER III

A BRIEF REVIEW OF CERTAIN FUNDAMENTAL CONSIDERATIONS UNDERLYING THE STUDY OF ACUTE HEMORRHAGE IN MAN

THE clinical as well as the experimental study of acute hemorrhage must be based on a foundation of physiological data. The determination of the total amount of blood in the body, its specific gravity and coagulation time, the amount which an individual may lose and recover, with and without treatment, and, closely related with the last, its regeneration after hemorrhage must all be considered.

The Total Amount of Blood in the Body.—The estimation of the total amount of blood in the body of an individual has a practical as well as a theoretical importance. In cases of acute hemorrhage the knowledge of the total amount of blood as calculated for any given individual, when compared with the amount of blood lost, would immediately give a basis for both treatment and prognosis. In performing transfusion of blood in nonhemorrhagic cases the question at once arises as to how much blood can be safely withdrawn from the circulation of the recipient before replacing it with blood from the donor. In hemorrhagic cases it is of great assistance to have any data which will bear on the question as to how much blood to transfuse—too little not benefiting the patient as much as possible, and too much tending to do harm. Moreover, in experimental work situations often arise in which

accurate knowledge of the total amount of blood would be of great value.

According to Allen Moulin, one of the first to study the question, the total blood mass equals one twentieth the body weight. Hoffman believed it to be one fifth, while Lehman and Weber in their experiments on two decapitated criminals determined it to be one eighth. Hayem obtained variable results in experimenting on dogs, his figures ranging from one eighth to one and one half twelfths. He therefore considered that there is considerable variation in normal animals. Dastre states that Buntzen, Léon Fredéricq, and Dogiel also give one and one half twelfths as representing the total amount of blood for dogs, and cites an experiment of his own in which he determined the amount to be greater than that. Stewart and Howell both give one thirteenth, and this has been the most commonly accepted fraction during recent years.

In some recent work of Haldane and Smith in which the total blood mass was determined by making the person examined inhale a measured amount of carbon monoxid gas, determining the oxygen capacity of the blood, and comparing the result with the determined oxygen capacity of a given amount of ox blood, they found in the fourteen normal cases studied that the total blood mass varied between one sixteenth and one thirtieth of the body weight. If their method may be accepted as accurate, it is evident that the total amount of blood is smaller than has been heretofore believed, and that it varies over quite a wide range in different individuals.

From the foregoing it must be concluded that with our present knowledge the question is still under judgment. The very nature of the problem makes it a difficult one to solve, and at the best the statement that the ratio between the total blood mass and the body weight is a constant one must be considered to be only very roughly approximating the truth.

The Amount of Blood which an Individual may Lose, and Survive.—According to Cabot, women can endure a greater hemorrhage than men, and children may succumb to a comparatively slight hemorrhage. Individual variation makes a great difference in the ability to withstand hemorrhage. No exact amount of blood can be stated as the maximum that anyone may lose and yet survive. Tillmans agrees substantially with Cabot, and says: "After severe loss of blood every surgeon has seen in a relatively short time—two to three days—threatening symptoms vanish in cases where he expected certain death; and again, on the other hand, some patients go into collapse after the loss of very little blood. Very young children may be endangered by an insignificant hemorrhage, and weakly children a year old have died after the loss of only 250 gm. of blood. In strong adults, who are otherwise healthy, the loss of half the total amount of blood is sure to be fatal. Women appear to stand the loss of blood better than men. The formation of new blood seems to take place more easily and rapidly in them on account of the periodic replacement of the blood lost in every menstruation (Landois). Fat people and old and weak individuals are very susceptible to the loss of blood. The more rapidly the hemorrhage takes place the more dangerous it is."

Howell says that a healthy individual may recover without serious difficulty from a loss of as much as three per cent of the body weight of blood, but that the exact per cent which may be lost has not been determined.

Vierordt states that dogs recover from a hemorrhage of from 2 to 3 per cent of the body weight easily, while a loss of 4½ per cent, which he considers to be more than one half the entire blood, would probably be fatal.

Hayem found that the removal of one nineteenth the body weight of blood from healthful adult dogs was always fatal,

while if one twentieth were removed a certain number survived. On the other hand, Stewart states that an animal may recover after losing considerably more than half its blood. Taylor and Frazier found that about 40 per cent represents the maximum loss that a dog will survive even after prompt intravenous injection of saline solution. According to Béchamp, dogs will endure a loss of blood equal to 3 or 4 per cent of the body weight, while Huenerfauth gives 3½ to 4½ per cent. Hall and Eubank, from whom the above is quoted, believe that the limit doubtless varies with different individuals.

It is evident from the difference of opinion of the various writers above referred to that it is impossible to say exactly how much blood an animal may lose and yet survive. As we cannot determine the exact amount of blood in proportion to the body weight in any given animal by the application of any simple calculation, it is equally impossible to calculate the amount that may be lost even as an average for a given number of cases. Consequently in any given case we can only guess with rough approximation what would be a fatal loss.

The Specific Gravity of the Blood.—According to Cabot, the specific gravity of the blood is of interest chiefly because of its bearing a definite relation to the amount of hemoglobin in the blood. Schmaltz has worked out tables which express this, and his results have been confirmed by Yarrow in a later research. Jones studied the specific gravity of human blood under different normal and pathological conditions, and found that it varies with age and sex and different individuals, and that it is lowered by eating, raised by exercise, gradually lowered during the day, and gradually raised during the night.

Cabot gives the normal specific gravity of human blood as 1.059, but the more commonly accepted figure is 1.055. According to Howell, in the adult human male it may vary from 1.041 to 1.067, and the average is about 1.055.

The Coagulation Time of the Blood.—To quote Howell, the coagulation time of blood varies in the normal individual according to circumstances, and it also varies slightly in different normal individuals. As he states it "under normal conditions the blood passes into the jelly stage in from three to ten minutes." According to determinations based on the use of Wright's tubes the normal coagulation time of human blood is about three minutes. As is well known, pathological conditions may increase the coagulation time very much, as, for example, in cases where there is obstruction in the biliary tract with resulting jaundice.

Cabot states that the coagulation of the blood increases in rapidity the greater the amount of blood is lost, and thinks that this is due in all probability to the increase in the number of blood plates which different observers have noted after hemorrhage. He also states that after severe hemorrhage coagulation occurs almost instantly. In the experiments on dogs recorded in these pages it has often been noticed that the blood coagulates more quickly after an acute hemorrhage than under normal circumstances.

The Formation of New Blood in the Body after Acute Hemorrhage.—According to von Mikulicz, the regeneration of lost blood to complete restoration to the normal depends on the amount of blood lost, the age and nutrition of the patient, the methods of treatment, and the coexistence of other disease. Other conditions being favorable, he says that the loss is made up as follows:

1. Less than 1 per cent of the blood mass in two to five days.
2. From 1 to 3 per cent of the blood mass in five to fourteen days.
3. From 3 to 4 per cent of the blood mass in fourteen to thirty days.

Bierfreund noticed that after operations for malignant disease the blood does not begin to regenerate until considerably later than after other operations. It was a week later on the average, and it never reached as high a point as before the operation. In 72 cases of malignant disease he noted the percentage of hemoglobin every day after the operation in order to ascertain how long it took for the hemoglobin to rise. He found that in ordinary operations the blood began to be regenerated in from five to twenty days.

TABLE OF BIERFREUND'S—BASED ON SEVENTY-TWO CASES

DIAGNOSIS	Per cent Hgn. Before Operation	After Operation	LOSS	Time Before Hemoglobin Rose
Malignant tumors:				
No complications.	68.5	53	15.5	23 days
Very large or rapidly growing tumors.	56.6	38.4	18.2	27.8 "
Tumors with softening or marked disturbance of function.	57.5	39.7	17.8	27.0 "
Average.				25.9 "

Kiefer concluded after seven experiments, mostly on cats, that in some cases after hemorrhage the diminution of the amount of hemoglobin was greater than the diminution in the number of corpuscles, and that in the regeneration of the blood it took longer for the hemoglobin to return to normal than for the red corpuscles. He also found that in the first few days after an acute hemorrhage there is a continued diminution in the red cells and hemoglobin.

For the account of the observations of the author on the regeneration of blood after acute hemorrhage, as studied from the donors used in the transfusion cases, the reader is referred to Chapter IV.

CHAPTER IV

THE SYMPTOMS OF ACUTE HEMORRHAGE, COMPARISON OF THE SYMPTOMS OF ACUTE HEMORRHAGE AND OF SHOCK, AND THE DIFFERENTIAL DIAGNOSIS OF INTERNAL CONCEALED HEMORRHAGE AND SHOCK

Study of the Clinical Symptoms Following Severe Bleeding of a Recipient Just Before Transfusion.—The following detailed account of a preliminary bleeding and subsequent transfusion well illustrates the symptoms of acute hemorrhage of severe degree. (For the full case history, see Case IV, 4 (7,117), page 372.) The patient was transfused for the third time for inoperable carcinoma of the groin as a means of last resort after all hope of recovery had been abandoned. In order to replace as much of the old blood as possible, the preliminary bleeding was carried as far as it was felt that it could be and leave a margin of safety. The observations during the operation were made by one person, who devoted his entire attention to the task, in order to obtain as great accuracy as possible. Particular attention is called to the fact that the account of the transfusion is as valuable in the study of hemorrhage as the hemorrhage itself, as the former merely reversed the order of the appearance of the symptoms of the latter.

Case No. IV, 4 (7,117).

1.19.—Pulse, 120. Respirations, 20. Began to bleed patient from right radial artery in the cubital fossa.

1.20.—Hemoglobin, 95 per cent. The method of Tallqvist was used, and the blood was taken as it spurted from the radial artery.

1.25.—Blood-pressure, 112 mm. This was taken from the upper arm with a Riva-Rocci apparatus, using a broad cuff.

1.27.—Pulse (radial), 144 per minute.

1.29.—Blood-pressure, 100 mm.

1.30.—Pulse, 160. The change in pressure was plainly appre-

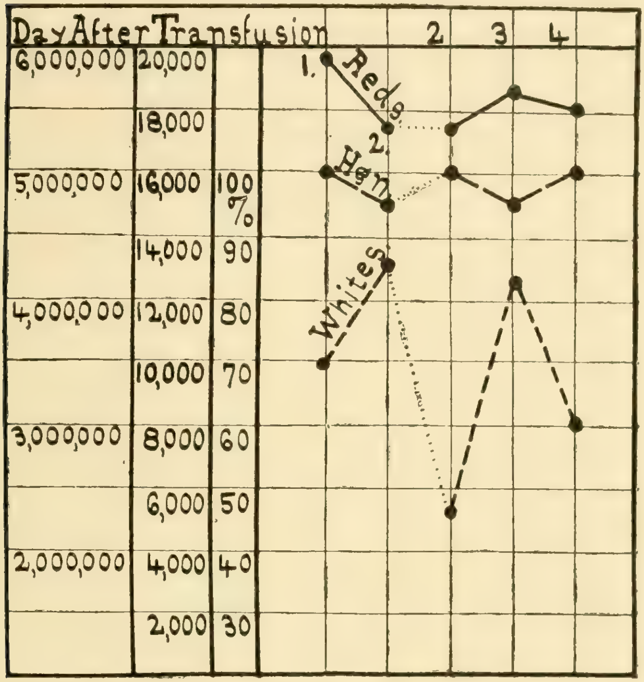


FIG. 8.—CASE NO. II, 1, (6599). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, forty-eight minutes. Note *early* fall in red cells and hemoglobin, and *early* rise in white cells.

ciable by the finger. The action was regular, and the volume steadily diminishing. At about this time the patient was raised slowly a little in a modified Trendelenburg position, in order to keep the heart well supplied with blood. This was increased as the bleeding went on.

1.30½.—Pulse, 160.

1.32½.—Blood-pressure, 90 mm.

1.35.—Hemoglobin, 85 per cent.

1.40.—Hemoglobin, 75 per cent. This change was plainly shown,

and, if inclined to be observed with inaccuracy, the error was toward the conservative side, i. e., the observation may have been a little lower than was estimated.

1.41.—Pulse, 160.

1.42½.—Hemoglobin, 75 per cent.

1.44.—Respirations beginning to show the effect of the bleeding—shallow, rate about 30 per minute.

1.46.—Pulse, 164.

1.47½.—Hemoglobin, 75 per cent.

1.48½.—Respirations shallow, rapid, and gasping. There was slight restlessness, and the lips were noticeably paler.

1.50.—Stopped the bleeding. Total amount of blood removed, 1,650 c.c. The patient complained of being nauseated, was very pale, somewhat sweaty, and the skin of the face and upper chest was cold. The face was deeply wrinkled, and looked old and careworn.

1.53.—Began slowly to infuse normal saline solution.

1.55.—The patient suddenly passed into a rather critical condition. The face was bathed with cold sweat, the respirations were very rapid, he complained a great deal about his leg hurting him, and the carotid pulse could not be obtained at all, even after repeated trials. This may have been due in part to the restless movements of the patient's head and the corresponding movements of the neck muscles. The pallor seemed to be increased, and there was more of a dirty, grayish hue to the skin.

1.58.—Hemoglobin, 70 per cent. The patient was very thirsty, and drank water greedily, but only in small amounts at a time.

2.03.—The respirations shot up from about 50 to 88 per minute, and were extremely shallow and gasping. The face was most drawn and anxious and much wrinkled. The coldness of the face continued, and also the profuse sweating. About 20 minims of adrenalin, 1–1,000, were given intravenously in divided doses.

2.06.—The breathing became rather paroxysmal, and was quieter. The patient was less restless, and more inclined toward stupor.

2.09.—Began to transfuse.

2.11.—Respirations, 60, and of better quality.

2.15.—The respirations suddenly began to get more rapid, and went up to 76. The heart sounds could not be heard at all with the stethoscope, but this was not positive indication that the heart was not beating, as the respirations were very rapid and noisy. The saline solution was being given during all this time. To relieve the heart the patient's feet were lowered a little.

2.25.—The patient opened his mouth wide every time he breathed, indicating marked air-hunger. He was slightly nauseated. He began to raise a little frothy sputum. His voice was almost aphonic.

2.27½.—The pulse as taken from the exposed radial artery was 150, very weak, and slightly irregular. No further exact blood-

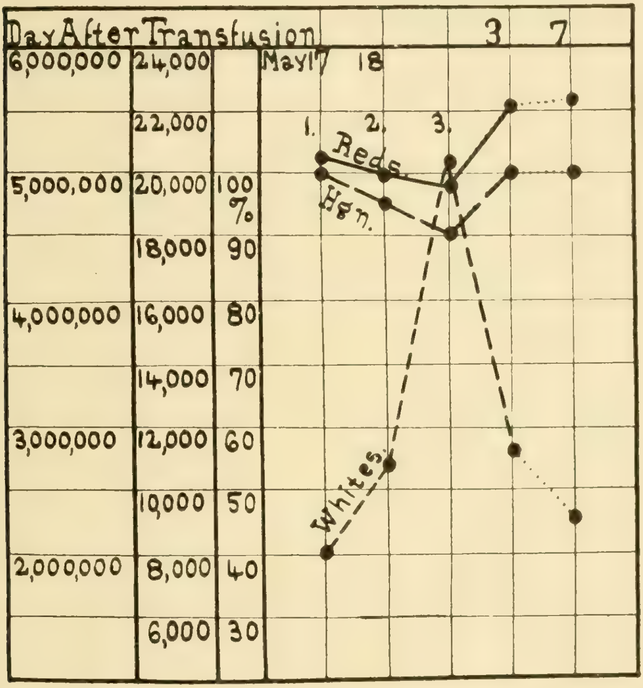


FIG. 9.—CASE NO. III, 3, (6853). BLOOD CHART OF DONOR. 1. The day before transfusion. 2, 3. Just after, and seven hours after. Duration of transfusion, twenty minutes. Note moderate fall in red cells and hemoglobin, and marked rise in white cells.

pressure observations could be taken on account of the apparatus interfering with the operative part of the transfusion, and also on account of the condition of the patient.

2.29.—Pulse of better volume and tension, and regular. A slight amount of frothy mucus was raised occasionally. There was occasional slight coughing. The face was fuller, less wrinkled, and indicated a beginning dilatation of the peripheral vessels.

2.30.—Respirations, 44, and of better quality. Face fuller and redder. Frothy sputum still raised.

2.30½.—Pulse decidedly irregular.

2.31.—Pulse irregular; rate, 165.

2.33.—The bowels moved involuntarily. The saline infusion was stopped; total amount given, about 1,000 c.c.

2.35.—Percussion showed the line of cardiac dullness to be about half an inch over the right border of the sternum, owing to acute dilatation of the right heart. The heart sounds still could not be distinguished with the stethoscope. The pulse, as felt in the exposed radial artery, was weak and irregular. The patient's face was fuller and of a dusky red color.

2.36.—The radial pulse was not transmitted at about every twentieth beat. Rate, 166. Several doses of digitalin (gr. $\frac{1}{50}$) were given subcutaneously.

2.37.—The right heart was still further dilated—about one inch from the sternum. The face was less full and the dusky redness began to diminish.

2.37½.—The respirations were 40, and easier. The color of the face continued to improve.

2.39.—The pulse was of better volume and tension. The heart seemed to be a little less dilated.

2.42.—Pulse, 140. Less sputum raised.

2.45.—Pulse, 136; much better volume and tension. The face was beginning to have much more nearly its original color. The general condition was much better. The patient did not feel apprehensive. He breathed more easily, although still at the rate of 40 per minute. The right heart was definitely less dilated. The skin was not as cold, and there was less sweat. The partial stupor had almost all passed away.

2.49.—The transfusion was stopped. Total duration, forty minutes.

2.52.—Pulse, 140.

2.58.—Hemoglobin from blood from ear lobe, 85 per cent. The wounds were bandaged.

3.02.—Respirations, 42. Pulse, 136, regular, better tension.

3.06.—Face much more natural. The intense redness was all gone and replaced by a nearly natural hue. The patient still complained of being thirsty.

3.15.—The patient complained of feeling chilly. Preparations for the second transfusion were begun. The breathing was much easier, but at the same rate. No more frothy sputum was raised.

3.21.—Began the second transfusion. By this time the patient was in a horizontal position which he had been allowed to reach by degrees in order to relieve the acutely dilated heart.

3.22.—Pulse, 128. As the fresh supply of blood began to show its effects the patient's head and trunk were raised in order to still further relieve the heart and prevent further dilatation.

3.24.—The patient still complained of feeling chilly.

3.25.—A slight chill began, and more blankets were asked for.

3.27.—Pulse, 128, of much better tension, regular, and of better volume.

3.27½.—Still thirsty, and was given a small amount of water.

3.30. — Respirations, 40. Much quieter and more composed. Still shook from the chill. The face began to lose its normal redness and to become gray—probably due to the chill causing (or accompanying?) contraction of the peripheral blood-vessels. This was just the opposite of the condition caused by the acute dilatation of the heart and pulmonary edema, in which the face was puffy and dusky red.

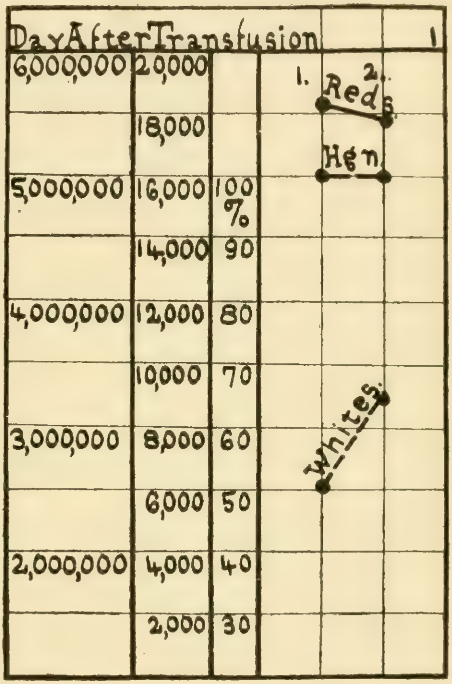


FIG. 10.—CASE NO. IV, 1, (6850). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, eight minutes. Note *early* slight fall in red cells, unaltered hemoglobin, and *early* proportionately marked rise in white cells.

3.33.—Pulse, 136.

3.36.—Respirations, 40, and possibly a little more shallow.

3.38.—Pulse, 128, of good volume and tension, and regular.

3.40.—The patient still complained of being cold, but the tremors of the face, arms, and chest muscles were less marked. Very thirsty, and was given water.

3.43.—Pulse, 132. There was slight coughing, and a slight amount of frothy sputum was raised.

3.46.—Respirations, 42.

3.47.—The face, for the second time, began to fill out again and resume the color it had before the chill. This was probably due in part to the increased amount of blood in the vessels, and also to the chill being markedly diminished. The voice was still weak and husky.

3.48.—The chill was still less apparent—both subjectively and objectively.

3.51.—Patient very thirsty. Complained of his leg hurting a good deal, and suggested morphin for relief. Was slightly restless. Respirations, 40.

3.53.—Pulse, 120.

3.55.—Pulse regular; tension and volume good. Slightly more restless, and as this was thought to be due in part to his having received enough blood, as well as to the discomfort in the hip, the transfusion was stopped. Duration of the second transfusion, thirty-four minutes.

4.00.—Hemoglobin, 90 per cent. The patient laughed and joked with those around him, and said that he felt very much better, although he was still troubled by pain in his hip. His face was normally full, his skin warm, and not sweaty, and his respirations easy, although still 40 per minute.

Summary.—(1) Total amount of blood removed, 1,650 c.c. (2) Total amount of normal saline solution given subcutaneously, about 1,000 c.c. (3) Duration of the first transfusion, forty minutes. (4) Duration of the second transfusion, thirty-four minutes.

Symptoms of Acute Hemorrhage.—The symptoms of acute hemorrhage are due to *diminution in the volume of the circulating blood, and to the physiologic effects of the resulting anemia.*

Among the symptoms due to diminution in the volume of the circulating blood is the general shrinkage of the body. This is most noticeable in the face and hands. In the face the lines of expression are deepened, the orbital spaces are shrunken, the nose is pinched, and the lips are thinned—the entire face is actually shrunken. In the hands the shrinkage

is similarly noticeable, especially of the backs and the finger tips near the nails.

Loss of blood volume also causes well-marked changes in the circulation. The chambers of the heart being less dis-

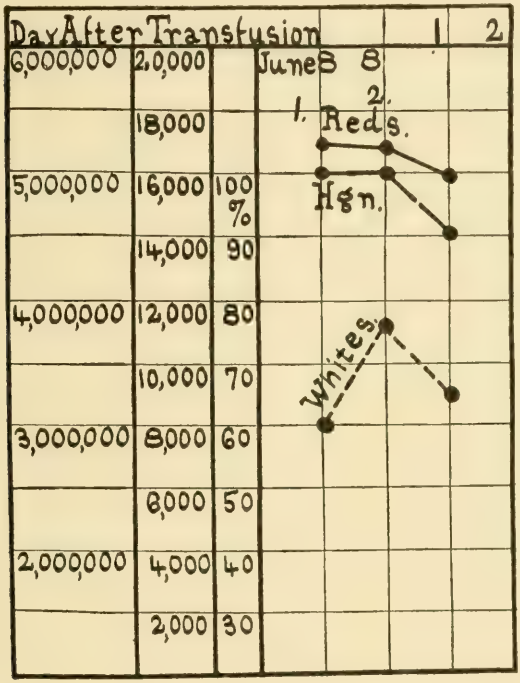


FIG. 11.—CASE NO. IV, 3, (6899). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion about thirty-five minutes. Note delayed fall of red cells and hemoglobin and *early* proportionately marked rise of white cells.

tended, the pulse volume becomes smaller and the rate quicker. A natural consequence is pallor of the skin and mucous membranes. In the laboratory, on playing bleeding and transfusion against each other, the heart rate, the pulse volume, the color of the skin and mucous membranes, and the volume

of the general body tissues may, within certain limits, be altered at will.

The phenomena caused by altered physiologic functions due to anemia of the various tissues and organs are more numerous and complex. For the purposes of this chapter only some of the grosser and more apparent alterations of function will be considered—viz., those of the circulatory and central nervous systems.

In the circulatory system the particular cardiac factor of great practical importance is that of the potential capacity of the myocardium. The blood stream pumped through the coronary arteries shares the general reduction of tension caused by the loss of blood. Hence the heart muscle is less efficiently nourished, and can do less work. The extent of disability bears a certain relation to the degree and duration of the anemia. Therefore, when the critical stage of hemorrhage has been reached and relief is most urgently needed, the heart is not only less able to respond, but is more readily additionally or totally impaired by drug stimulation or by a too rapid increase in the volume of circulating fluid following introduction of substitutes for blood, such as normal saline, Ringer's, or Locke's solutions, or introduction of transfused blood. It is obvious that direct myocardial changes are less important as symptoms than as guides to the manner of treatment.

In anemia the central nervous system is the weakest link among the various parts of the body which form the vital chain. The phenomena of anemia of the central nervous system are of the highest importance both in diagnosis and prognosis. Of these the ones attendant on anemia of the respiratory and the higher cerebral centers are the most important.

Diminution in volume of the circulating blood causes

diminution in the amount of oxygen carried to the respiratory centers. Consequently these centers are proportionately stimulated, just as they are in asphyxia. The result is an increase in the respiratory action in the effort to compensate for the loss of oxygen. When marked, this compensation

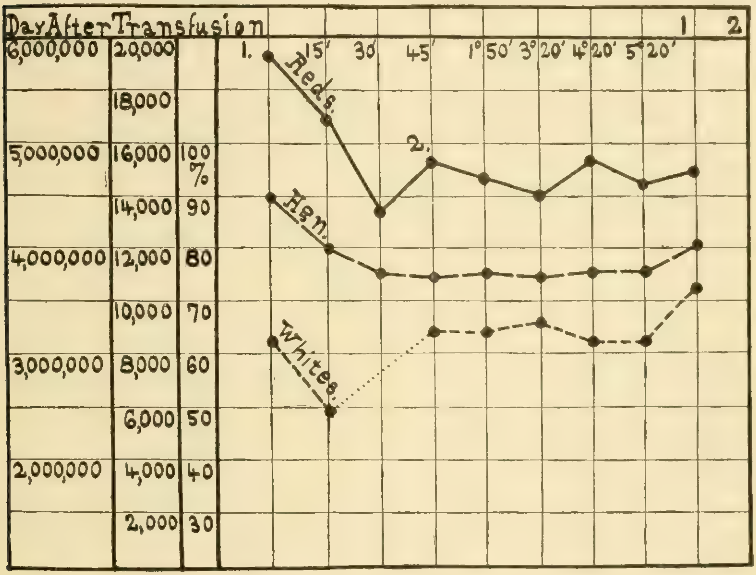


FIG. 12.—CASE NO. VI, 1, (2047 L). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, forty-four minutes. Note *early* marked fall in red cells and hemoglobin, and early fall in white cells with rise soon following. The early fall in the white cells was probably due to the rapidity of the bleeding.

produces the state known clinically as "air hunger." The efficiency of the circulation through the respiratory centers being virtually the same as that of the circulation of the remainder of the central nervous system, and the results of the alteration of the circulation of the respiratory centers being so easily observable, it follows that the respiratory

8

changes furnish the most accurate index of the gravity of the hemorrhage.

Not only is the respiratory rate of importance, but also, and in the early stages of hemorrhage, the respiratory rhythm. An occasional deep inspiration or a sigh may be noticed even before changes in the pulse are observable. For the most part this is the first warning from a donor to stop transfusing.

The appearance of psychic phenomena first express the response of the higher cerebral centers to anemia. The early reaction of the motor centers of brain and cord are shown by restlessness of the patient.

From the foregoing it is seen that altered rhythm and rate of respiration, psychic disturbance, and restlessness are the primary symptoms of anemia of the central nervous system. For practical purposes of diagnosis the finer and less obvious changes, such as in the special reflexes, changes in mental power, vasomotor power, and voluntary muscular power, and many others need not be considered here.

In the effort at compensation for the lost volume of blood, fluid is rapidly taken up from the general body tissues. Since this fluid contains no red blood cells, the red count and the hemoglobin fall. As it requires a certain time for transference of fluid from the tissues to the blood stream the changes in the hemoglobin and red count appear later than the symptoms due to loss of blood volume and to anemia of the central nervous system. Since the transference continues after cessation of the hemorrhage, the hemoglobin and red count may continue to fall after cessation of the hemorrhage. Finally, since the transference of fluid increases the volume of the circulating fluid, the general symptoms may be improving while the red count and hemoglobin are still falling, the fall being a relative one only. For this reason changes

in the hemoglobin and red count may appear measurably later than the other phenomena. On the other hand, the white count rises almost immediately, and usually continues to rise *during* a progressive hemorrhage (this should not be con-

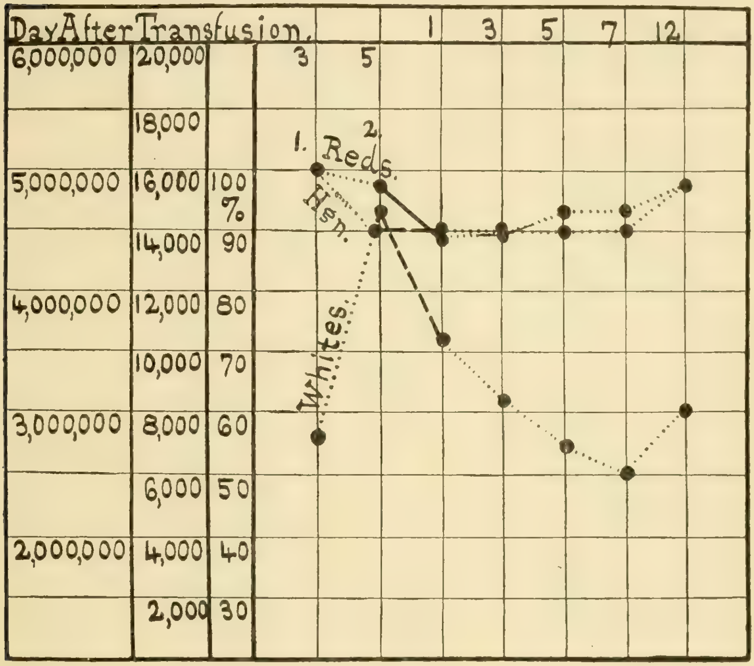


FIG. 13.—CASE NO. VII, 2, (6698). BLOOD CHART OF DONOR. 1, 2. Two days before, and just after transfusion. Duration of transfusion, twenty-five minutes. Note moderate *early* fall of red cells and hemoglobin, and marked *early* rise of white cells.

founded with the fact that the *maximum* rise usually occurs shortly after the hemorrhage has ceased). Hence a rising white count is more nearly a contemporary occurrence than a fall in the hemoglobin or red count.

Summary.—The physical evidence of loss of blood volume —namely, the actual shrinkage of the face and hands, the

pallor of the skin and mucous membranes, the diminished volume and the increased rate of the pulse, the altered physiologic functions of the central nervous system (altered rhythm and rate of respiration, psychic changes, restlessness), as well as a rising white count—these manifestations form the great primary symptoms of acute hemorrhage. Following these are a falling hemoglobin and red count, sweating, thirst, alterations in the special senses, and many minor symptoms, all of which constitute valuable supporting evidence.

Sequelæ of Cerebral Anemia Incidental to Acute Hemorrhage.—In another series of experiments besides those described in these pages, Dr. D. H. Dolley and the author have repeatedly demonstrated the interesting and very important relationship of acute cerebral anemia to the preservation of the functions of the brain and spinal cord. They have shown that any or all of the higher centers of the brain of a dog cannot undergo the loss of their blood supply for a longer period of time than six or seven minutes without being permanently injured or completely destroyed. This is proved not only by the changed symptoms of recovery animals after chloroform or asphyxia death for varying lengths of time with complete cessation of circulation and respiration and then resuscitation by suitable means, but also by the formation of demonstrable and constant changes in the structure of the central nervous system. Cessation of the circulation causes cerebral anemia, and the functional and organic changes vary according to its duration. At one extreme of cerebral anemia may be cited the rapidly transient but none the less evident effects caused by " fainting "—i. e., temporary cerebral anemia —and at the other the permanently changed nature of animals which have been resuscitated after comparatively long intervals of circulatory inactivity.

These facts have a most practical bearing on resuscitating

people after apparent death from any cause, and on many other conditions which the surgeon is called on to treat. In his thesis written in 1898, Demetrius Malliotis chose as his subject "Les Troubles Visuels Graves après les Pertes du Sang," and collected a number of illustrative examples. He concludes that

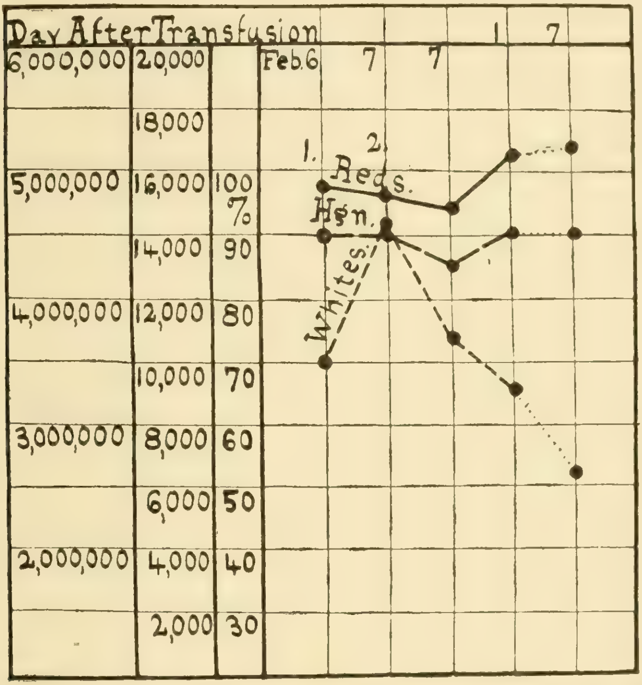


FIG. 14.—CASE NO. VII, 3, (6696). BLOOD CHART OF DONOR. 1, 2. The day before, and just after transfusion. Duration of transfusion, nineteen minutes. Note slight fall of red cells and hemoglobin, and *early* proportionately marked rise of white cells.

amblyopia and amaurosis may follow hemorrhages of any kind, that the former may assume the simple form, although exceptionally the hemeralopic and hemianopic forms, and that the condition is a very serious one. These cases present clinical evidence of injury of the brain or of the retina due to

anemia, and show that such injury may be localized. This subject will be considered fully at a later time and in another place.

NOTE.—Since going to press Proell's article has appeared in the "Medizinische Klinik." In the short time since then it has been impossible to obtain a copy of the original article, but the abstract appearing in the "Journal of the American Medical Association" is as follows: "Proell comments on the 198 cases in the literature in which optic neuritis terminating in atrophy followed excessive loss of blood, and reports a case personally observed. Choked papilla entailing almost total blindness came on in a few days after excessive menstrual hemorrhage in a girl of sixteen, previously apparently healthy, the third time that the menses had occurred. No cause for the excessive hemorrhage could be determined; it was arrested only by tamponing the vagina on the sixth day. Vision improved later in one eye so that the patient can now count fingers at six feet, but the other eye is totally blind. Proell thinks that there must always be some blood affection or nutritional disorder at the basis of these severe visual disturbances after loss of blood, remarking that he knows of no instance of the kind in healthy soldiers after hemorrhages. In only 12.4 per cent of the total number on record was the amaurosis unilateral, but the degree of disturbance frequently varied in the two eyes, the right being more severely affected in 85.7 per cent. In a few instances the amaurosis came on suddenly and was complete in both eyes—in these cases the patients generally woke in the night with severe headache and found themselves blind as in the case reported. There is one case on record of sudden total deafness (!) from the same cause. Treatment can only be dietetic and tonic measures to restore strength and to supply the missing juices to the organism. Injections of strychnin and galvanism are perhaps indicated to maintain the excitability of the optic nerve. On account of the bad prognosis disturbances in vision following great loss of blood are to be feared as much as blindness after the use of quinin, wood alcohol, or other poison."

Comparison of the Symptoms of Acute Hemorrhage and of Shock.—In order to compare the symptoms of acute hemorrhage with those of shock, the following description of a patient in shock, as written by the author for Keen's "Surgery"

(page 937), is given. The symptoms which may occur in acute hemorrhage are italicized, while any added statements in regard to hemorrhage are placed in parentheses:

"The symptoms of a patient in shock, as resulting, for instance, from a severe injury of the extremities in which the loss of blood may be inconsequential, may be stated as follows:

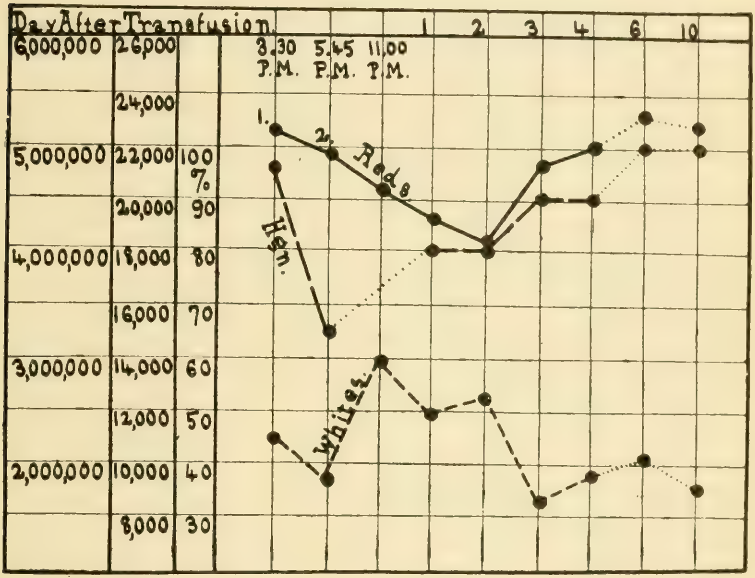


FIG. 15.—CASE NO. VIII, 1, (6695). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, thirty-six minutes. Note *early* moderate fall of red cells and very marked fall of hemoglobin, and initial slight fall with later rise of white cells.

The patient *lies quietly and indifferently upon his back* (late stage), and *in severe cases he may remain in the position in which he has been placed by the bystanders.* The *face is pale,* sometimes cyanotic (rarely), elongated, *shrunken, pinched,* and *devoid of movements* (late stage). The *eyes are shrunken,* either *staring or half closed* (late), the *cornea is lusterless,* the *pupils dilated,* and *reacting but torpidly to light* (late particu-

larly). The *lips* are *thin and slightly separated* (with air-hunger they may be widely so); the *natural redness is absent.* The *extremities are cold.* The *muscular movements may not be abolished* (they are increased at first) but are *markedly diminished* (late). Only occasionally is a *feeble movement*

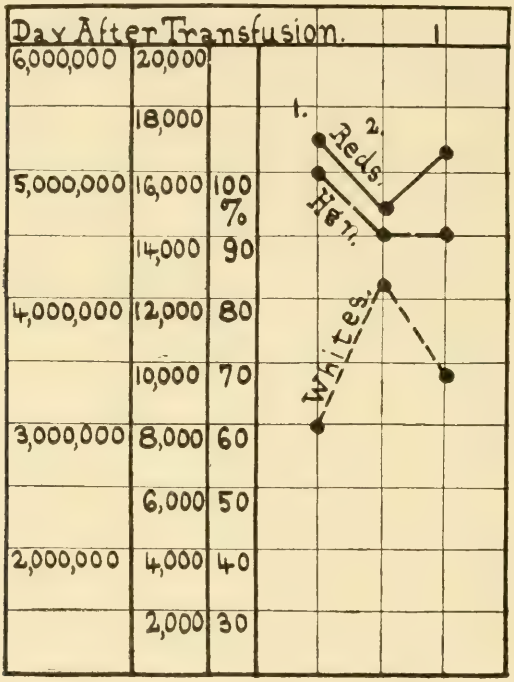


FIG. 16.—CASE NO. VIII, 4, (6849). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, thirty-one minutes. Note *early* fall in red cells and hemoglobin, and *early* rise in white cells.

attempted (late), or a *groan, weak and hoarse,* interrupts his *deathlike silence* (the noise varies according to the stage). *The reflexes still persist,* but are *greatly diminished* (vary according to the stage). The *general skin surface is pale,* but at the peripheral parts, such as the fingers and toes, there is sometimes slight cyanosis (rarely present), and *cold, clammy*

sweat—most marked on the forehead—transudes from the pores. The *respiration is superficial, shallow, and irregular, frequently interrupted by a sighing expiration.* The *temperature may show a decrease* of from one to two (seldom more than three) degrees Fahrenheit. The *pulse is weak,* its *frequency is* usually (always) *increased,* though occasionally it may be decreased. The *sensibility* and all the *special senses are impaired.* The patient is *apathetic* (late) and gives the impression of *utter indifference to his surroundings and his own condition* (late). He *fails to respond* to commands or entreaties to move or to answer questions addressed to him (late). The *mental stupor is only too apparent* (late). In severe cases *unconsciousness completes the picture* of this pseudo-death. The *sphincters fail to functionate* (occasionally); *incontinence of the feces* is a frequent occurrence (occasionally occurs), that of the urine more seldom. *Nausea, vomiting,* and *singultus* may be present. Deglutition may be present."

On the whole there are but two facts which stand out at all clearly as showing a difference between severe acute hemorrhage and profound shock. The first is that the preliminary stage of excitation of hemorrhage is usually absent in shock. The second is that the pulse rate in hemorrhage is always increased—at least the author has never witnessed a slowed rate in many observations. The diagnostic value of these two differences is much reduced on account of the exceptions which occur. In the exceptional cases the last hope of making a differential diagnosis between shock and hemorrhage from the symptoms is thus apparently completely removed.

Why should there be such a striking resemblance between the manifestations of the two conditions? It is perfectly apparent when it is remembered that in hemorrhage the blood is permanently lost from the vessels, while in shock it accumu-

lates so largely in the large venous trunks, particularly of the splanchnic vessels, that it is of as little use in maintaining the blood-pressure as if it were actually outside of the body. When the bleeding occurs into the abdominal cavity, the most frequent seat of internal concealed hemorrhage, the two conditions

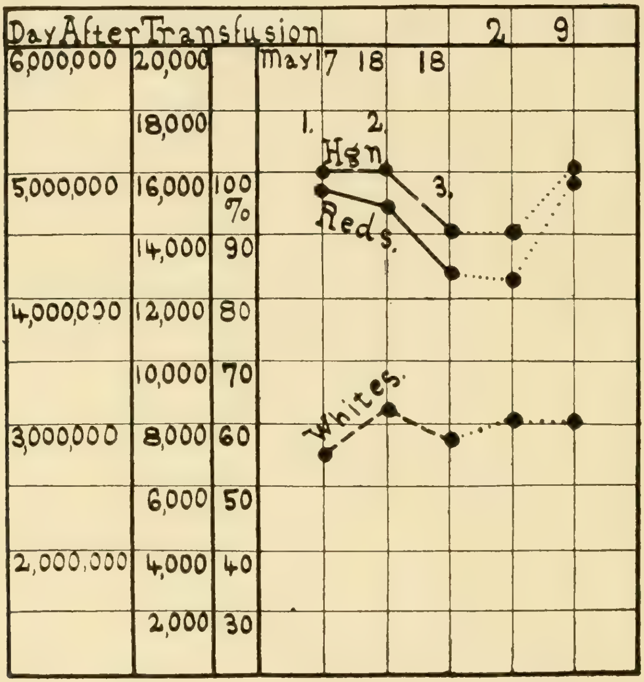


FIG. 17.—CASE NO. VIII, 6, (6898). BLOOD CHART OF DONOR. 1, 2, 3. The day before, just after, and seven hours after transfusion. Duration of transfusion, twenty minutes. Note very slight *early* fall in red cells and unchanged hemoglobin, and *early* slight rise in white cells.

vary only in the fact that in one case the blood is outside the vessels and in the other inside.

Differential Diagnosis.—The question of the differential diagnosis between internal concealed hemorrhage and shock, especially when both conditions exist at the same time, as not

infrequently happens, is an important one. In the absence of a history of traumatism, the presence of visible bleeding, or the presence of free fluid in the large body cavities, the author believes that the diagnosis cannot with certainty be made without a series of carefully made blood examinations. Even if a history of traumatism be given, it may be of no help in making the diagnosis. It is obvious, therefore, that if characteristic changes occur in either or both conditions in the composition of the blood, a basis is afforded for making a differential diagnosis. In the experimental work described in Chapter II it has not only been shown that definite changes occur after acute hemorrhage, but also that definite and different changes occur in shock. In man it is ordinarily very difficult to obtain opportunities to make careful examinations in such cases. All that usually can be done is to provide for the immediate necessities of the patient. An excellent opportunity has been afforded by the clinical cases of transfusion to study the immediate blood changes of acute hemorrhage in the donors as the conditions were under control in all details.

Studies of the Immediate Effects of Acute Hemorrhage as Made from the Donors in Clinical Transfusions.—The symptoms were studied in 60 donors. In 18 cases detailed observations were made of the red corpuscles, the white corpuscles, and the hemoglobin. In the other cases the study of the general symptoms was of equal value, so that the material from which the deductions have been made is quite large. What has been previously said about the similarity of the symptoms of shock and acute hemorrhage was fully confirmed.

Red Corpuscles.—In 17 cases out of 18 the number of red corpuscles per cubic millimeter was reduced in amount varying with the length of the transfusion and the amount of blood that was lost. The reduction occurred from prac-

tically immediately after, up to seven hours after the transfusion. In Case No. IX, 1 (6,411), Second Donor, there was a fall of 1,500,000 cells by the end of the transfusion, which lasted twenty-eight minutes—a comparatively short time.

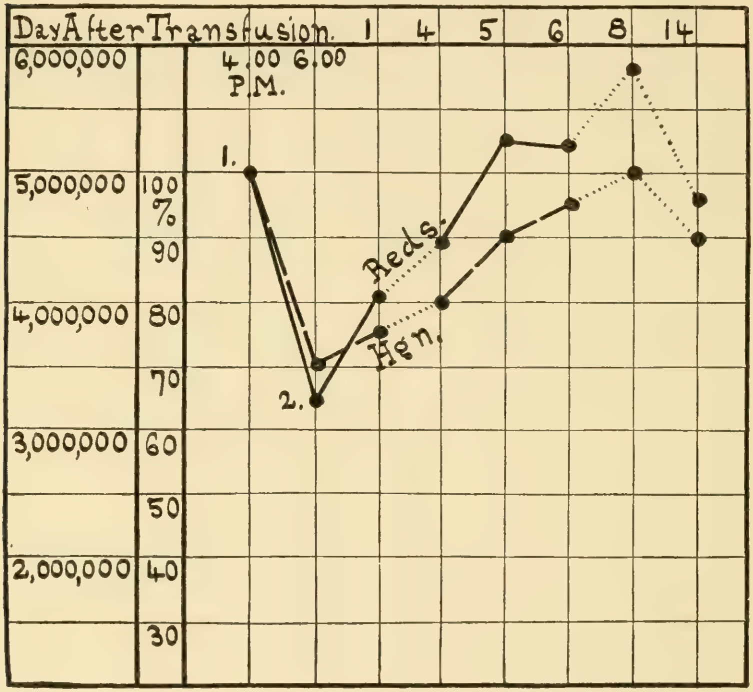


Fig. 18.—Case No. IX, 1, (6411). Blood Chart of First Donor. 1, 2. Before, and shortly after transfusion. Duration of transfusion, twenty minutes. Note *early* very marked fall in red cells and hemoglobin.

Three hours after the transfusion a fall of a little over 2,000,000 cells had occurred. This was the greatest fall that was observed. In 5 cases the fall was slight or very slight, and in one case the level was unchanged.

Hemoglobin.—In 12 of the 18 cases the hemoglobin had fallen within a short time after the transfusion, while in the

remaining 6 it was unaffected then, although there was usually a fall later. In most of the cases the fall occurred at the same time that the fall in the red cells did, while in a few others it came a short time after the initial fall in the red calls. The greatest fall recorded was that in Case No. IX, 4 (6,492), in which the maximum was reached in six hours and twenty minutes with a loss of 40 per cent.

White Corpuscles.—The observations on the white corpuscles were made in 13 out of the 18 cases. In 12 of these 13 cases they rose immediately after the transfusion, while in the remaining 1 there was a slight initial fall which may have been due to the vigor of the bleeding causing an actual reduction before those in the tissues could pass into the blood stream in sufficient numbers to cause the relative rise which came later. The most important fact which was observed was that the *maximum* rise occurred very *early*, either almost immediately, or in a very short time. The range of increase varied from 1,000 to 2,000 up to the maximum in 1 case of 26,000 (Case No. IX, 9, 6,663), a most striking change to occur by the end of the bleeding of fifty-four minutes. In Case No. III, 3 (6,853), the immediate rise was sharp, and the maximum was not reached until after seven hours had passed, but this was the longest time required to reach the maximum in any case. The reaction of the white corpuscles to the hemorrhage did not die down immediately in any case, so that the original level was reached on the same day, but usually took from one to five days to do so (see individual charts).

The detailed consideration of the blood changes in the 18 cases is as follows:

Case No. II, 1 (6,599).

Observations were made immediately before the transfusion at about 10.30 A.M., and then at night (exact time not given). In this

interval there was a loss of 552,000 red cells per cubic millimeter, a fall in hemoglobin of 5 per cent, and a rise in the white cells of 3,600 per cubic millimeter. Here again the red cells showed the most marked change, while there was too little change in the hemoglobin

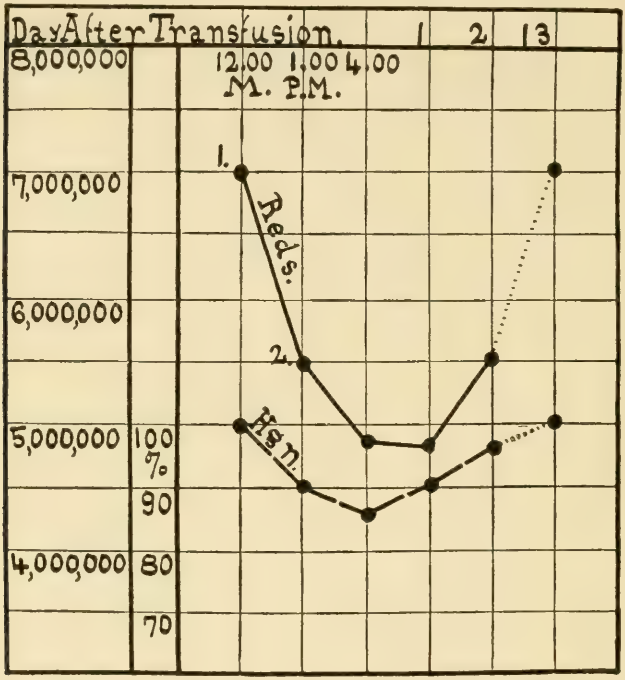


FIG. 19.—CASE NO. IX, 1, (6411). BLOOD CHART OF SECOND DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, twenty-eight minutes. Note *early* very marked fall in red cells and much less marked fall in hemoglobin.

and white cells to be of particular significance. Earlier changes of greater amount may have been lost through no earlier observations having been made. (See Fig. 8.)

CASE NO. III, 3 (6,853).

Comparing the observations made the day before the transfusion and immediately after, the red cells were found to have fallen 140,000 per cubic millimeter, the hemoglobin 5 per cent, and the white cells to have risen 2,750. Seven hours after the transfusion the red cells

had fallen 230,000 below the original point, the hemoglobin 10 per cent, and the white cells had risen 12,360—a marked rise. (See Fig. 9.)

Case No. IV, 1 (6,850).

The changes in this case were very slight, but as the transfusion only lasted eight minutes under good arterial pressure, they are of value as illustrating what may happen in so short a time. The red cells fell 100,000, the hemoglobin was unaffected, and the white cells rose 2,890. Unfortunately, only two sets of observations were made. Considering the short time, the reaction of the white cells was rather marked. (See Fig. 10.)

Case No. IV, 3 (6,899).

The transfusion lasted about thirty-five minutes. At the end of that time the red count was practically unaltered, having only fallen 40,000 cells per cubic millimeter. The hemoglobin was unaffected, and the white cells had risen 3,000. By the next day the red cells showed a total fall of 260,000, the hemoglobin of 10 per cent, and the white cells had fallen to within 1,000 of the original level. As in several other cases in which there was slight change in the red count and hemoglobin, the white cells reacted much more vigorously, and very shortly after the transfusion was over. (See Fig. 11.)

Case No. VI, 1 (2,047 L).

Even in as short a time as the first fifteen minutes after the transfusion began there were marked changes in the blood, as shown by the reduction of the red cells of 608,000 per cubic millimeter and of the hemoglobin of 10 per cent. The white cells also fell to 2,800—an unusual occurrence in man, but one which occasionally occurred in dogs. Soon after this, at forty-five minutes, they had risen again 3,200 per cubic millimeter, which brought them to a point slightly above that at which they were at first. At this same time the red cells had begun to rise a little, although over a million lower than at the start, and the hemoglobin was 15 per cent lower than at the start. The duration of the transfusion was forty-four minutes. (See Fig. 12.)

Case No. VII, 2 (6,698).

The preliminary counts were made two days before the transfusion. The observations made immediately after the transfusion showed a loss of red cells of 120,000 per cubic millimeter, and a gain

in white cells of 7,240 per cubic millimeter. The hemoglobin showed a loss of 10 per cent. The reaction of the red cells and hemoglobin was much less marked than the sharp rise of the white cells, and was sluggish throughout. (See Fig. 13.)

CASE No. VII, 3 (6,696).

The preliminary observations were made on the day before the transfusion. The white count was slightly increased, but shortly

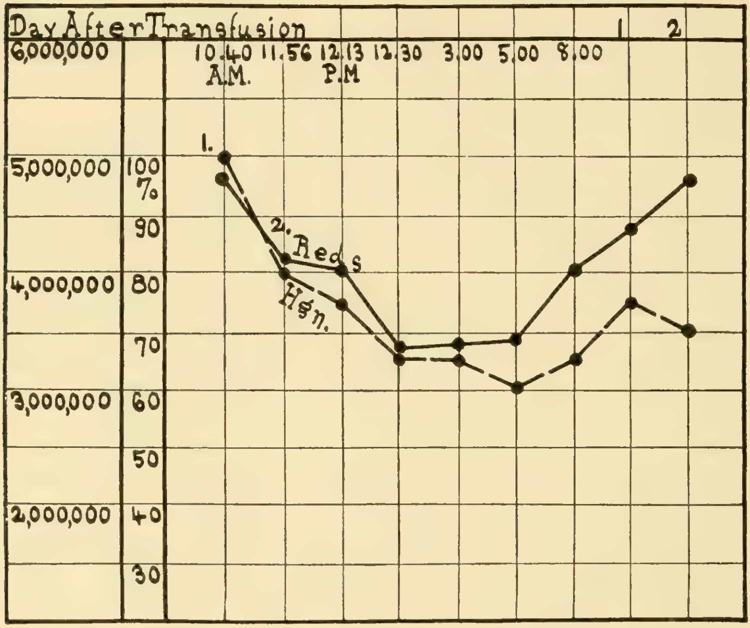


FIG. 20.—CASE No. IX, 4, (6492). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, fifty-six minutes. Note *early* marked fall in red cells and parallel fall in hemoglobin.

after the transfusion (the exact time was not noted) it had risen 4,000 per cubic millimeter. At the same time the red cells had fallen 80,000 per cubic millimeter, while the hemoglobin remained unchanged. In this case the slight changes may probably be accounted for, at least in part, by the fact that the transfusion only lasted nineteen minutes and that the donor was an unusually strong and full-blooded individual. (See Fig. 14.)

CASE NO. VIII, I (6,695).

The transfusion lasted thirty-six minutes. Two and one quarter hours after the beginning of the transfusion the red cells showed a fall of 264,000 per cubic millimeter, the hemoglobin a fall of 30 per cent, and the white cells a fall of 2,080 per cubic millimeter. Five and one quarter hours later the white cells had risen 5,240 (3,120 higher than before the transfusion), so that their rise was delayed. (See Fig. 15.)

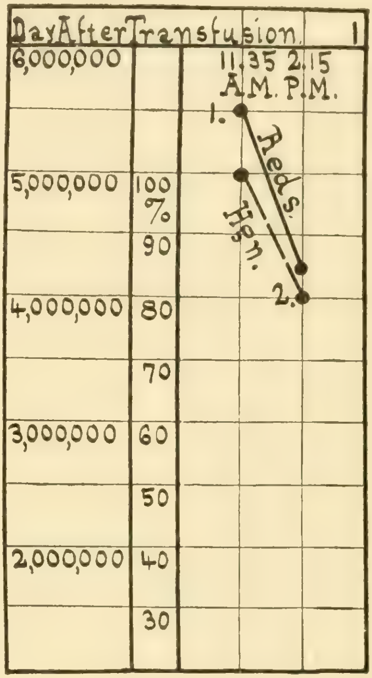


FIG. 21.—CASE NO. IX, 5, (6539). BLOOD CHART OF DONOR. 1, 2. Immediately before, and shortly after transfusion. Duration of transfusion, forty-five minutes. Note *early* marked fall in red cells and parallel fall in hemoglobin.

CASE NO. VIII, 4 (6,849).

Observations were only made just before and after the thirty-one-minute transfusion and on the following day, but while few in number, they are of value in illustrating the immediate changes which took place. The red cells fell 564,000 per cubic millimeter, and the hemoglobin 10 per cent. The white cells rose sharply 4,400 per cubic millimeter. The changes were consistent and typical. (See Fig. 16.)

CASE NO. VIII, 6 (6,898).

Immediately after a transfusion which lasted twenty minutes, the red count had fallen 140,000, the hemoglobin was unaffected, and the white count had risen 1,480. Seven hours later the red count had fallen a total of 680,000, the hemoglobin 10 per cent, and the white count had fallen to within 1,000 of the original level. (See Fig. 17.)

CASE NO. IX, I (6,411). FIRST DONOR.

The observations were made immediately before the transfusion and in less than two hours after it was finished. In that time the

red cells showed the marked fall of 1,800,000 per cubic millimeter, and the hemoglobin a fall of 30 per cent. Unfortunately, white counts were not made, as it would have been of interest to see how great a reaction there would have been after such marked changes in the other two elements. The transfusion lasted twenty minutes. A large amount of blood passed over with the comparatively slight fall in the blood-pressure of 27 mm.—less than would have been expected. This case well illustrates how impossible it is to determine before a transfusion how much blood will be lost in a given time. Too many factors influence the problem, some of them variable and some fairly constant, to enable the exact weight of each to be calculated. (See Fig. 18.)

Case No. IX, 1 (6,411). Second Donor.

As with the other donor used in this case, a brother of the present one, the changes in the blood were very marked. The transfusion lasted twenty-eight minutes. Within thirty-two minutes after it stopped, the red cells showed a fall of 1,540,000, with a fall in the hemoglobin during the same time of only 10 per cent. By the end of three hours the red cells had fallen a total of 2,196,000, and the hemoglobin a total of 15 per cent. The unusually high red count of the donor permitted a much greater loss than could otherwise have been borne with as little functional disturbance as he showed. That his general condition was excellent was shown by the lost red cells and hemoglobin being replaced by the end of thirteen days. Possibly they were replaced sooner, as no observations were made between the second and thirteenth days. No white counts were made. (See Fig. 19.)

Case No. IX, 4 (6,492).

No observations were made of the white cells. One hour and sixteen minutes after the transfusion began the red cells showed the marked fall of 752,000 per cubic millimeter, and the hemoglobin a loss of 20 per cent. In one hour and fifty minutes after the transfusion began the red cells had fallen altogether 1,456,000 per cubic millimeter, and the hemoglobin 25 per cent. These results are very clear and very striking, and occurred in a comparatively short time. (See Fig. 20.)

Case No. IX, 5 (6,539).

The white cells were not counted. The red cells and hemoglobin were observed immediately before the transfusion, which lasted forty-

five minutes. Two hours and twenty minutes after the transfusion began (one hour and fifty minutes after it ended) the number of red cells had fallen 1,245,000 per cubic millimeter, and the hemoglobin 20 per cent. (See Fig. 21.)

Case No. IX, 8 (6,854 and 6,957). First Donor.

This case seems to be one of the exceptions which prove the rule. The transfusion lasted twenty minutes. Sixteen minutes after

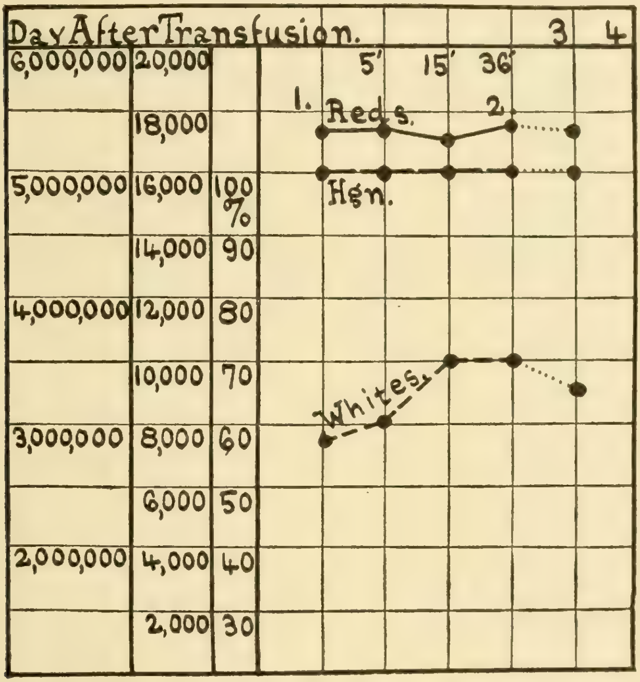


Fig. 22.—Case No. IX, 8, (6854 and 6957). Blood Chart of Donor. 1, 2. Just before, and sixteen minutes after transfusion. Duration of transfusion, twenty-nine minutes. Note unchanged red cells, and hemoglobin, and slight rise in white cells at end of thirty-six minutes. (See explanation in text).

it stopped the red count and hemoglobin determination were unchanged, while the white cells showed a rise of 2,560 per cubic millimeter. The lack of fall in the red cells and hemoglobin is explained by the fact that the compensation was very strong, as shown by the

rise in the blood-pressure of the donor from 135 to 150 millimeters of mercury. If further observations had been made on the same day (they were not made until the third day after the transfusion) a fall

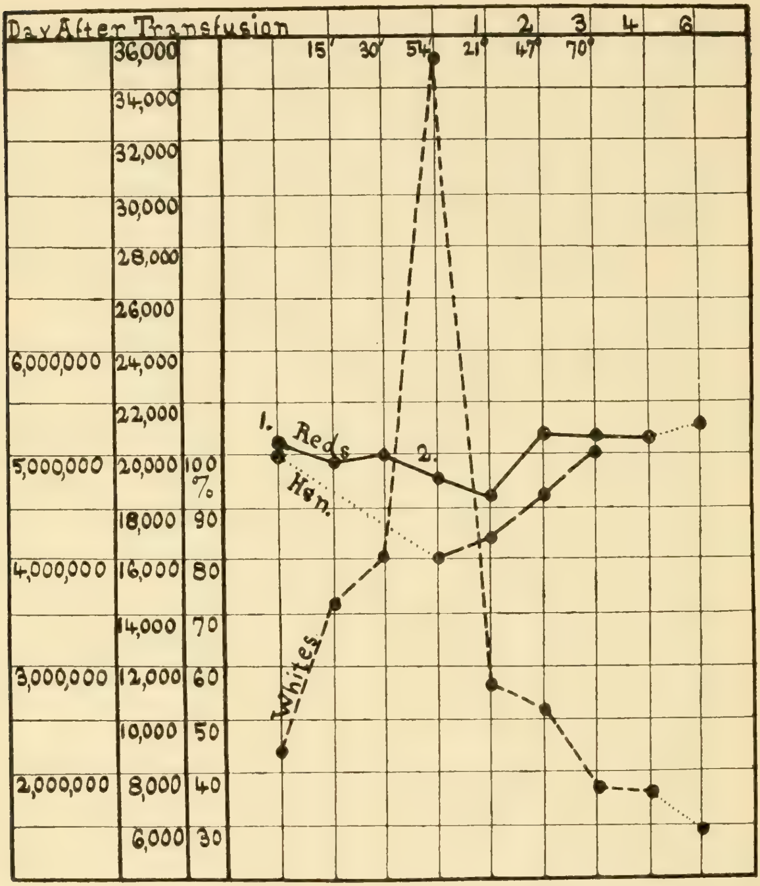


FIG. 23.—CASE NO. IX, 9, (6663). BLOOD CHART OF DONOR. 1, 2. The day before, and just after transfusion. Duration of transfusion, fifty-four minutes. Note moderate fall in red cells, marked fall in hemoglobin, and very marked rise in white cells—all by the end of the bleeding of fifty-four minutes.

in the red cells and hemoglobin would doubtless have been shown, because the lymph would have passed from the tissue into the blood stream to make up the loss of blood-plasma, and the blood would have

been diluted until regeneration of the lost corpuscles had occurred. If the unusually strong compensation had been broken down by a more prolonged and severe bleeding, the changes would have been shown immediately. (See Fig. 22.)

CASE No. IX, 9 (6,663).

The curves plotted from the observations made in this case are very striking. No observations were made immediately before the transfusion, but they were made on the previous day, and showed a

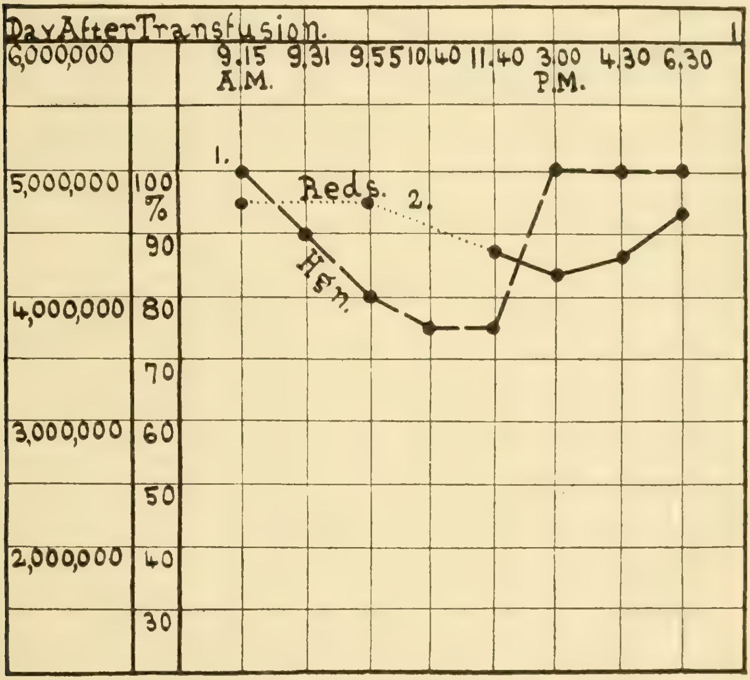


FIG. 24.—CASE NO. IX, 11, (6538). BLOOD CHART OF DONOR. 1, 2. Just before, and just after transfusion. Duration of transfusion, fifty-five minutes. Note *early* moderate fall in red cells and more marked fall in hemoglobin.

normal blood. Within the first fifteen minutes after the transfusion began there was a loss of 180,000 red cells per cubic millimeter (a fall in the hemoglobin cannot be stated to have occurred in the same time, as no observation was made until later), and there was a gain of 5,580 white cells per cubic millimeter. The red and the white

cells were counted at the end of thirty minutes, the former being still further decreased and the latter still further increased, and at the end of fifty-four minutes there was a loss of red cells of 308,000 per cubic millimeter, a fall of 20 per cent in the hemoglobin, and an increase in the white cells of 26,460 per cubic millimeter. The duration of the transfusion was fifty-four minutes. (See Fig. 23.)

Case No. IX, 11 (6,538).

In this case there was a steady fall in the red corpuscles and the hemoglobin. The white cells were not counted. The transfusion lasted fifty-five minutes. Before the transfusion was over (thirty-five minutes after it began) there was a slight fall of the red cells of 24,000 per cubic millimeter, and a marked fall of the hemoglobin of 20 per cent. One hour and twenty minutes after it began the hemoglobin was down to 25 per cent (the red cells were not counted at this time), and two hours and twenty minutes after it began (one hour and twenty-five minutes after it ended) the hemoglobin was still down 25 per cent, and the red cells had fallen 746,000—a marked fall. (See Fig. 24.)

Case No. XI, 1 (6,855).

After a transfusion which lasted twenty-four minutes, the fall in red cells was only 28,000 (a difference which might easily occur between two blood counts made from the same blood by the same observer), the hemoglobin was unaffected, and the white cells showed the greatest reaction—a rise of 3,000. At the end of seven hours the red cells had fallen a total of 348,000, the hemoglobin 10 per cent, and the white cells had fallen slightly from the previously reached maximum level. (See Fig. 25.)

From the operative standpoint, it is obvious that changes such as occurred in the above instances would be of diagnostic value only if they took place in a reasonably short time after the onset of the bleeding, and also if they occurred under such circumstances that they could be accurately observed. With a patient possibly bleeding to death, every minute of delay increases the operative risk. In order to show the time limitation as clearly as possible the following table has been compiled:

The Immediate Effects of Acute Hemorrhage on the Composition of the Blood Remaining in the Body

Case No.	Time of Observation After Transfusion	Reds	Hemoglobin	Whites
II, 1 (6599)	Shortly after.	Fell.	Fell.	Rose.
III, 3 (6853)	Shortly after.	Fell.	Fell.	Rose.
IV, 1 (6850)	Shortly after.	Fell.	No change.	Rose.
IV, 3 (6899)	Shortly after.	Fell very slightly.	No change.	Rose.
VI, 1 (2047L)	Shortly after.	Fell.	Fell.	Rose sl.
VII, 2 (6698)	Shortly after.	Fell slightly.	Fell.	Rose.
VII, 3 (6696)	Shortly after.	Fell slightly.	No change.	Rose.
VIII, 1 (6695)	Not more than 135 minutes.	Fell.	Fell.	Fell.
VIII, 4 (6849)	Shortly after.	Fell.	Fell.	Rose.
VIII, 6 (6898)	Shortly after.	Fell very slightly.	No change.	Rose sl.
IX, 1 (6411) First Donor.	Not more than 120 minutes.	Fell.	Fell.	....
Second Donor.	Not more than 60 minutes.	Fell.	Fell.	....
IX, 4 (6492)	Not more than 20 minutes.	Fell.	Fell.	....
IX, 5 (6539)	Not more than 165 minutes.	Fell.	Fell.	....
IX, 8 (6854 and 6957)	Not more than 15 minutes.	No change.	No change.	Rose.
IX, 9 (6663)	Not more than 54 minutes.	Fell.	Fell.	Rose.
IX, 11 (6538)	Not more than 60 minutes.	Fell.	Fell.	....
XI, 1 (6855)	Shortly after.	Fell very slightly.	No change.	Rose.

Summary:

The Red Cells.

18 observations.

Fell 17 times (5 slightly or very slightly).

Unchanged 1 time.

The Hemoglobin.

18 observations.

Fell 12 times.

Unchanged 6 times.

The White Cells.

13 observations.

Rose 12 times (2 slightly).

Fell 1 time.

From all of the foregoing facts the conclusion is that in the normal healthy individual the loss of a moderate amount of blood at a fairly rapid rate will be quickly followed by definite progressive changes in the blood remaining in the body.

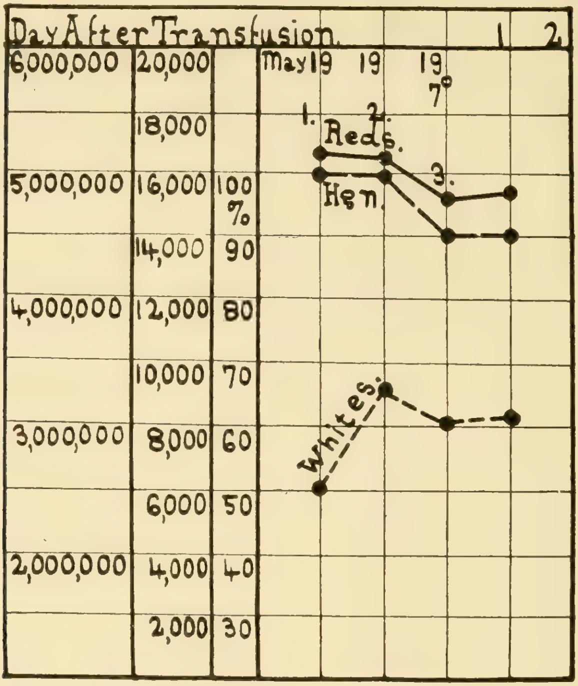


FIG. 25.—CASE NO. XI, 1, (6855). BLOOD CHART OF DONOR. 1, 2, 3. Just before, just after, and seven hours after transfusion. Duration of transfusion, twenty-four minutes. Note practically no *early* change in red cells and hemoglobin, and proportionately marked *early* rise in white cells.

These changes vary in extent according to the amount of blood lost and the rapidity of the flow, but in the average case one would always expect to find (1) a fall in the number of red cells per cubic millimeter, (2) a decrease in the percentage of hemoglobin, and (3) an increase in the number of white cells per cubic millimeter, with the *maximum*

increase occurring *early*. In shock there is no fall in the hemoglobin, no fall in the white count, and no fall in the red count. The establishment of these facts should be of assistance in making a differential diagnosis between internal concealed hemorrhage and shock when it is impossible to do it in any other way, it being recognized that both conditions are essentially progressive in character and therefore requiring serial determinations from which to draw deductions.

CHAPTER V

PATHOLOGIC HEMORRHAGE: HEMOPHILIA AND PURPURA

THE three chief groups under which so-called pathologic hemorrhages fall are (1) hemophilia, (2) purpuric conditions, and (3) those associated with obstructions of the bile ducts. In the last of these the condition is known to be due to the presence of bile salts in the blood, and different observers have proved that active hemolysis may occur as a result. As purpuric and icteric conditions present practically the same problems, the latter will not be discussed in detail.

Hemophilia.— In his "Practice of Medicine," 1901 edition, Osler defines hemophilia as a "constitutional fault, hereditary or acquired, characterized by a tendency to uncontrollable bleeding, either spontaneously or from slight wounds, sometimes associated with a form of arthritis." Since this was written it has been generally accepted that the associated arthritis is a manifestation of hemorrhage into the joints, and that it is therefore of purely hemophiliac origin.

Heredity.—The influence of heredity in hemophilia is well known. Kinnicutt has summarized the facts as follows:

1. As a rule, the daughters of a bleeder father are exempt from evidence of the disease, but transmit it to their male offspring.

2. The sons are also as a rule exempt, but do not transmit it to their offspring.

3. The daughter of a bleeder father may transmit the disease to a single one, to several, or to all her offspring.

4. Where there are several daughters, the capability of transmission to offspring may be confined to a single one, or all the daughters may transmit it.

5. Occasionally there is direct transmission from father to son through several generations.

6. The disease does not appear in the issue of the sons of a bleeder family who are not themselves bleeders.

However, there is not always evidence of the presence of any hereditary influence so far as can be discovered by careful investigation of the history of the ancestors of the patient, his immediate family, or his immediate relatives. Weber, Townsend, Müller, Bates, and others have reported such cases.

Occurrence.—Hemophilia is of more common occurrence in males than in females. In Grandidier's 212 cases there were 197 males to 15 females, a ratio of about 13 to 1. In the cases reported in the literature between 1889 and 1899 Stempel found 167 males and 42 females, or a ratio of about 4 to 1. Apparently there has been an increase in the number of females affected since Grandidier's time, or else, as Stempel suggests, more cases have been recorded, and the ratio more truly shown in consequence. He quotes Kehrer and Fagge as giving 13 to 1, Legg 11 to 1, and Comby 10 to 1.

Certain families have become bywords in the medical literature of hemophilia through their affliction extending back over so long a time in different generations. Notable among these is the Appleton-Swain family, which is referred to by Osler, and which was reported by Hay in the early part of the nineteenth century. In this family the disease is said to have existed for nearly two centuries. Otto describes a family in which it could be traced back for eighty years. The Mampel family of Kirchheim, stated by Weil to have been reported by Chelius in 1827, by Malzenbrecher in 1841, and by Lossen in 1876 and 1904, furnishes another example of the hereditary

nature of this disease. Out of 212 members there were 111 males, and of these 37 were hemophiliacs, all the females being free from this affliction. Muir reports a family in South Africa in which hemophilia has existed for eight generations.

Etiology.—In spite of our knowledge of the different manifestations of hemophilia, we do not yet know what causes it. Various theories have been advanced, but none satisfactorily explains the condition. Some authors think it is of infectious origin, others that it is due to changes in the innervation of the capillaries, while still others cover up their lack of exact knowledge by calling it a diathesis. Some consider that it is akin to scurvy, but Sahli, for example, does not believe so at all. Again it has been considered to be due to a discrepancy between the blood mass and the vascular capacity. From the standpoint of its treatment, the problem it presents by reason of the hemorrhages into the tissues and the outer world is similar to that presented by certain cases associated with icterus and purpuric hemorrhages, and in that way it is more or less closely related to those conditions, possibly more nearly so than we are aware from our present knowledge.

Apparently there is no typical *pathological anatomy* of hemophilia. Different investigators have reported changes in the vessel walls, such as narrowing of the lumena, amyloid degeneration, and fatty degeneration, but others have failed to find these changes. Again, enlargement of the spleen and cardiac atrophy and dilatation have been reported, but the findings are far from being constant.

The same lack of uniformity of the findings in the different elements in the blood also exists. This may be attributable in part to the examinations not having all been made at the same relative periods of time. Between the hemorrhages a very different picture would be presented from that shown immediately after or during a hemorrhage. Possibly this explains why some

observers have found an increase in the number of red corpuscles over normal and others a decrease.

In studying *the blood* from three different hemophiliac families, Sahli found a marked decrease in the percentage of neutrophilic white corpuscles and an increase in the number of lymphocytes. The total leucocyte count was normal or diminished, which would mean that there was both a relative and an absolute decrease in the number of polynuclear forms. In the two cases in which the examinations were made the blood platelets were diminished in number, but not beyond the normal limits. In one case the alkalinity of the laked blood, the residue from the serum, and the freezing point were found to be normal, and in another the fibrin content was normal. Cabot cites two cases of hemophilia in which the white corpuscles were persistently diminished in number, and in both of which the red corpuscles were considerably reduced. In one of the cases nosebleed was occurring daily when the examinations were made. He says that the blood platelets are sometimes very scanty in hemophilia. Wright found a reduced white count with a reduction of polynuclear forms, while in opposition to this Rosner found a leucocytosis.

In Coe's cases of hemophilia and purpura the one constant feature found after repeated blood examinations was the occurrence of a very small number of blood platelets. In one of his cases their sudden disappearance forty-eight hours before bleeding took place indicated that it was about to occur. Blood taken from another patient on the same day on which the most severe attack of epistaxis occurred that had occurred for months, showed a total absence of platelets, whereas they had previously been present, but in a much less quantity than normal.

The generally accepted fact about the *time of coagulation* of hemophiliac blood is that it is much increased over the nor-

mal, notwithstanding that observations to the contrary have been reported. Whether the delay is due to deficiencies in the composition of the blood itself, to changes in the vessel walls, or to both, is immaterial as far as it immediately affects the welfare of the patient. The fact remains that bleeding has often occurred which has taken hours, days, or weeks to control. Sahli believes that the apparently contradictory observations of the clotting time may be avoided by taking the blood for examination from a perfectly fresh prick, and not from a wound which has been bleeding for some time. If taken from the latter the clotting time will be found to be shorter than if taken from a fresh wound. In the work cited elsewhere in these pages it has often been noticed that the coagulation time of the blood of normal dogs has been shortened after acute hemorrhage, and it seems possible that the fact noticed by Sahli may be partly due to the influence of the hemorrhage, *per se,* on the clotting time of the blood remaining in the body.

Symptoms.—The first symptom which is apt to call attention to the existence of hemophilia is that of persistent hemorrhage following a cut or bruise. The bleeding may be external or internal, into the tissues, or into the large or small serous cavities. In the 334 cases cited by Grandidier the bleeding in 169 was from the nose; in 43 from some part of the mouth, not including the tongue; in 36 from the intestinal tract; 17 from the lungs; 16 from the urethra; 15 from the stomach; and in others from other parts of the body, such as the finger tips, eyelids, outer ear, tongue, scrotum, etc. Eröss had a case in which there was hemorrhage into the pleuræ and pericardial sac, and he, Gocht, Weil, and others had cases in which hemorrhage occurred into the abdominal cavity. H. Fischer, von Limbeck, and Berggrun cite cases in which the bleeding was into the brain, and there are several histories which point clearly to this from the nature of the symptoms without the

diagnosis having been made absolutely. Janeway had a fatal case in which the hemorrhage was into the spinal canal. Many cases are on record in which the hemorrhage occurred into the joints. Other symptoms are those of hemorrhage itself.

A striking feature of hemophilia is that the *traumatism* which causes the bleeding may be so slight, and yet the outcome may be fatal. Stempel collected 19 cases of bleeding after the extraction of teeth, with fatal results in 6 of them. In one of Vickery's cases the mother of a child suffering from hemophilia sometimes had to change the child's nightdress during the night on account of the amount of bleeding which occurred from mosquito bites. Other unusual causes of bleeding which have been recorded are cutting of teeth, leech bites, scratch from a cat, circumcision, a wound caused by "eating mealies on the cob" (Muir), and instillation of nitrate of silver into the eye. Often, however, no appreciable traumatism may be noticed, and the bleeding seems to be purely spontaneous.

The *joint manifestations* of hemophilia deserve particular consideration. Formerly it was believed that they were due to an intercurrent affection, and, as previously stated, it is only recently that their true nature has been recognized. Cases were diagnosed as acute rheumatic arthritis, acute synovitis, and, in those in which there had been several hemorrhages into a joint with permanent tissue changes, as tuberculosis. Fatal results have followed operations on the knee owing to the true condition not being recognized. The knee and elbow joints are the ones most often affected. The onset of hemorrhage into a joint may or may not be accompanied with slight fever. There is swelling, tenderness, and pain. The tissues are not affected, as the effusion is largely if not wholly composed of blood. Later, however, after repeated hemorrhages the capsule may become thickened, and lose its smooth glistening ap-

pearance owing to the deposition of unabsorbed fibrin. Delicate wavy tufts of tissue may become formed, and swing free from their anchorage to it. Later still the cartilage of the joint becomes eroded in a greater or less degree, and finally adhesions begin to form and a corresponding degree of ankylosis develops. In a case reported by Summers there was complete bony ankylosis of the knee joint with atrophy of the muscles and marked flexion of the leg.

Treatment.—As regards *general prophylaxis* in hemophilia the endeavor should be made to prevent its spreading by forbidding (1) the marriage of the females from hemophiliac families, whether afflicted with the disease themselves or not; (2) of male hemophiliacs; and (3) of nonhemophiliac males from hemophiliac families in which other males of the same generation have transmitted the disease.

As regards *individual prophylaxis,* great care must be taken to avoid all wounds of operative or other origin, however slight, and all contusions, especially of the joints. The child should be carefully guarded from infancy and with particular care during the early years. The serious results which may occur from the most trifling injury have already been indicated.

The *general treatment* should be aimed at producing the best possible hygienic surroundings for the patient. He should have nourishing and varied diet, plenty of milk, as suggested by the findings of Wright and Knapp, fresh air and sunshine, moderate and carefully guarded exercise, sufficient sleep—in short, everything which will most help the body to help itself.

The great danger from hemophilia being due to the uncontrollable hemorrhages, the *specific treatment* should be aimed at stopping them, and in treating the anemia due to their occurrence. The first part of the problem may be divided into two parts—treatment aimed at controlling the hemor-

rhages by local means, and that aimed at controlling them by constitutional means.

In treating bleeding from an accessible wound the first essential is to obtain firm pressure by means of a bandage applied over a pad. On the pad may be placed a variety of agents. Sahli recommends above all the use of gelatin, and he and other writers suggest the local use of adrenalin in the same way. He considers that ferric chlorid is useless, and that the effect of calcium chlorid, thrombokinase, and zymoplastic substances will depend on the clotting power of the blood outside of the vessels. Kinnicutt and others recommend the use of calcium chlorid in 0.5 per cent aqueous solutions, and also finely powdered chalk mixed with the same solution, or the addition to it of a solution of nucleoalbumen. Other things which have been used are a 4-per-cent solution of cocain hydrochlorate and the application of a stream of carbonic-acid gas.

Gage had two cases of epistaxis in hemophiliacs in which the bleeding was controlled completely by spraying undiluted hydrogen peroxid into the nose. Large, of Cleveland, uses hydrogen peroxid as a routine method of stopping postoperative hemorrhages of endonasal origin in nonhemophiliacs.

Davies reports having used a freezing spray of ethyl chlorid in several cases of extraction of teeth from hemophiliac patients. He had no failures in using it several times, and considered it to be very efficient. He states that the oozing blood freezes and forms a firm compress in the alveolar process which prevents further bleeding. He used ethyl chlorid bulbs of his own modification with the beaks bent at an angle which permitted the easy application of the spray.

Broca successfully treated a case of hemophilia with bleeding from the alveolus after the loss of a milk tooth with a local application of diphtheria antitoxin, the subcutaneous in-

jection of 20 c.c. of the same, and the administration by rectum of half a liter of normal saline solution. The bleeding, which had lasted for two days before he saw the patient, stopped immediately and did not return in twenty-four hours.

While local treatment is being carried on, constitutional treatment should be attempted. Many cases have been reported in which the internal use of calcium chlorid has been followed by cessation of the hemorrhages owing to the coagulation of the blood being increased. In others it has proved to be of little or no value, and the same may be said of gelatin by mouth or subcutaneously. Much seems to depend on the dosage of the former and the manner in which it has been given. There seems to be no doubt from the author's personal experience that giving too much increases the coagulation time instead of diminishing it, and that it cannot be given over too long a time, at least without intermissions, without incurring the same result. Moreover, it has been found that it may be of no value. Sahli says that the use of calcium chlorid and ergotin is uncertain, and warns against the subcutaneous injection of gelatin as being harmless but inefficacious. He considers that the internal use of adrenalin is contraindicated.

Coe has recently reported the treatment of 5 cases of hemophilia and purpuric conditions with calcium lactate with extremely good results, and much more uniformity and certainty of action than has been obtained with the chlorid. He found that 30 to 40 grains of the lactate given once or twice a week was usually sufficient for the chronic cases. All of his patients were directed to drink from one to two quarts of milk a day, following the idea of Wright and Knapp, who found that the ingestion of milk increases the coagulability of the blood. After the bleeding stopped he gave arsenic to stimulate the blood-forming organs.

Jones reports the successful use of liquor thyroidei in an

eight-year-old child who had extensive hemorrhages from the digestive tract due to hemophilia since infancy. Various remedies, including calcium salts, had failed to relieve. Four drops of the liquor were given three times a day for six weeks. There was a single hemorrhage two weeks after beginning treatment, but none other had occurred at the end of more than five months. Fuller reports two cases of hemophilia in which thyroid extract had apparently effected a cure, and a surgical case in which secondary hemorrhage from the prostate gland was apparently stopped by it.

P. E. Weil, however, has recently done very interesting and valuable work in controlling pathologic hemorrhages of hemophiliac and other origin by means of injecting comparatively small doses of fresh sera from similar or dissimilar blood, either intravenously or subcutaneously. As far back as 1882 Hayem, in writing under the title "De la transfusion du sang considérée comme moyen hémostatique," states that he experimented with different natural and artificial sera to determine their effect on the coagulation of blood. While he states that human blood was one of the least active of the agents which he used, he recognized its power to increase coagulability when injected in comparatively small amounts. Weil's work has been an extension of Hayem's observations.

Weil found that the injection of fresh sera from man, rabbits, and horses was equally efficacious in stopping pathologic hemorrhages. He used 15 c.c. if the injection were made intravenously, and 30 if subcutaneously, repeating the doses as needed at rather long intervals. He found that old sera were not efficacious, and to get the full therapeutic result serum must not be more than fifteen hours old. While he found serum from cattle (sérum bovin) to be very active, he also found that it was the only one which caused any accidents, and that occasionally the effect was violent—high fever, chills,

cyanosis, vomiting, severe headache, and rachialgia resulting.[1] The reader is referred to his various articles as giving the best idea of what he has been able to accomplish. In almost all his cases the hemorrhages were at least controlled better than by any other means, and in many cases the effect was specific.

The effect of the transfusion of blood in cases of pathologic hemorrhage is discussed in Part II of this book. Weil's use of fresh sera is the nearest approach to transfusion which has been made for such conditions. If transfusion proves to be efficacious it has the advantage over the injection of small amounts of serum alone, that when a patient is in collapse from repeated hemorrhages it not only causes the hemorrhages to stop, but affords strong stimulation and replaces the lost blood at the same time.

Purpura.—Purpura, like jaundice, is purely a symptom, and in itself does not constitute a disease. It is a condition in which the coagulation time of the blood is usually slowed, and, possibly largely as a consequence, there are hemorrhages of different degrees of severity into the skin, mucous membranes, and other tissues of the body. The amount of extravasation usually depends on the severity of the associated condition. Largely for the sake of convenience cases associated with purpura are classified according as they are mild, moderate, or severe in nature under the headings of purpura simplex, purpura rheumatica, and purpura hemorrhagica. Hemophilia may often be purpuric in nature, but the symptom-complex is sufficiently constant to entitle hemophilia being ranked as an

---

[1] In this connection the author wishes to sound a note of warning. As long as human serum has proved to be efficient, and human blood may easily be obtained by inserting a large hypodermic needle into any superficial vein (see Chapter XVI, Technic of Making Hemolysis Tests for method) it should be used rather than serum from animals in order to avoid risk of causing hemolysis. Weil has reported unfavorable results from using bovine serum only, but nevertheless the danger is present with other sera of dissimilar origin.

entity. This may also be true of Henoch's purpura, but the use of the word purpura in describing it is unfortunate, as it would seem, as in hemophilia, that purpura is only one of the manifestations of the condition.

Etiology.—The large number of conditions with which purpura may be associated in itself indicates the improbability that any single etiological factor accounts for its occurrence. The most probable explanation suggested by a perusal of the clinical manifestations is that there is an alteration in the blood itself, possibly due to destruction of the platelets, whether from the presence of toxins elaborated in the course of acute or chronic infections, or some of the wasting diseases, or as a result of the administration of certain drugs. At times a mechanical cause seems to explain its occurrence, but only in a very limited number of conditions. In connection with the alteration in the blood there are possibly more changes than those which affect the coagulation time; changes in the blood-pressure may exert a decided influence. If a high blood-pressure occurring in an individual with calcified arteries may bring about rupture of an artery, it would certainly seem reasonable to suppose that a high blood-pressure might be one of the causes in producing the extravasations in purpuric conditions, whether the blood passed out by small tears in the vessel walls or by diapedesis. In certain experiments in transfusing dogs, mentioned elsewhere in these pages, urticaria was seen to develop most rapidly immediately under the eyes of the observers performing the experiments. It occurred only when the pressure of the flow from the donor of the blood was very high. Owing to its occurring so rapidly, and in a very short time after the transfusions were begun, the only reasonable explanation seems to be that the cause was purely mechanical. In other cases in which hemorrhages occurred from some of the parenchymatous organs into the abdominal cavity under excessive trans-

fusion, it was clearly shown that even with an apparently normal animal the blood could be forced through the vessel walls.

Classification.—Osler classifies the conditions with which purpura may be associated as follows: (1) Infectious (pyemia, septicemia, endocarditis, typhus, measles, scarlet fever, small pox); (2) toxic (snake venom, copaiba, quinin, belladonna, mercury, ergot, the iodids); (3) cachectic (cancer, tuberculosis, Hodgkin's disease, Bright's disease, scurvy, senile debility); (4) neurotic (locomotor ataxia, acute and transverse myelitis, severe neuralgia, forms of hysteria); (5) mechanical (pertussis, epilepsy). He mentions, in addition to the above, other forms associated with Henoch's purpura, joint disturbances, peliosis rheumatica, and the severe form usually known as purpura hemorrhagica. There is much evidence to show that the latter is simply the result of an infectious process (Letzerich, Grissoli, Bateman, Petrone, Lockwood, Köhler, Silbermann, de Benedetti, and others). Whether or not the invading organism is the same in all cases, and thus justifying purpura hemorrhagica being regarded as a definite infection, is far from being demonstrated, and even if it were, the fact would remain that the purpura was purely symptomatic.

In a general way the *treatment* of purpura as a symptom has been the same as the treatment of hemophilia, and the main object sought has been to increase the coagulability of the blood. The lime salts, gelatin solutions, and adrenalin have occupied the leading places in the therapeutic list. In addition to these aromatic sulphuric acid and turpentine have perhaps been recommended more for purpura than for hemophilia. Experience has shown, however, that there is no specific, and while a remedy may act favorably in one case it may fail altogether in another.

CHAPTER VI

THE TREATMENT OF ACUTE HEMORRHAGE. HEMORRHAGE IN OPERATIONS

The treatment of hemorrhage is naturally divided into the treatment of acute and so-called pathologic hemorrhage. As the problems presented in each are usually different, although pathologic hemorrhage may become acute, the latter has been considered separately in Chapter V.

ACUTE HEMORRHAGE

In acute hemorrhage from any part of the body the source of the hemorrhage must be determined and appropriate surgical measures taken to prevent the continuance of the loss. Often in internal hemorrhage, especially that occurring into the abdominal cavity, it is impossible to determine the source, or, if it be known, circumstances may be such that it is impossible immediately to adopt radical measures without killing the patient. After the hemorrhage is stopped the attention must be turned toward helping the patient over the crisis brought about through the loss of blood. This may be done by therapeutic or mechanical means separately or in combination. As has been shown in preceding experiments, the giving of drugs in hemorrhage not only may be of no value, but may and often does cause positive harm. The heart under most circumstances will work if it has anything to work with, and needs blood or other suitable fluid rather than drugs.

Certain **therapeutic agents** may be useful in securing rest and in increasing the vasomotor action. To secure rest, morphin is the drug of choice on account of the thoroughness of its action. To secure immediate results it should necessarily be injected hypodermically. Strychnin and digitalis act upon the vasomotor system, but their effect is least when the hemorrhage is deepest. Moreover, in the deepest hemorrhage, strychnin and digitalis may unfavorably influence the heart. After the blood-pressure has been raised by saline solution, the action of strychnin is increased and its dangers diminished. The bloodless heart is like a free-running propeller. First give it something to push against and then, if necessary, start up the accelerating apparatus behind it, the medulla, with strychnin. That strychnin acts more efficiently after the blood-pressure is raised by saline solution is only proof of the truth of this logic, and, again, as shown in the converse by the fact that convulsions caused by strychnin may be effectively stopped by reducing the blood-pressure by bleeding. Adrenalin causes contraction of the peripheral vessels, thereby tending to mass the remaining blood in the central vessels. Adrenalin is a valuable agent, but it must be very cautiously used.

Among the **mechanical agents** the subcutaneous or intravascular administration of normal saline, Ringer's, or Locke's solution, especially with adrenalin of a strength of $\frac{1}{50000}$ or $\frac{1}{75000}$ when given with a slow continuous flow, has proved until recently to be the most efficient means at our command. One disadvantage is, however, that a sudden cardiac breakdown may occur. Moreover, the limitations are only too clearly shown by the experimental work and by numerous clinical cases in which a certain amount of improvement would be obtained, but the blood-pressure would then fall and a fatal termination soon follow. The explanation is easy to find in

the passage of the fluid out of the vascular system into the tissues, and also into the body cavities. A search through the literature reveals very few recorded cases of death due to the administration of too large amounts of saline solution, but questioning the pathologist of any large hospital will be apt to elicit the opinion that the autopsy findings after the administration of postoperative infusions show more fluid in tissues and cavities than is compatible with the opinion that the procedure is a harmless one. Fourmeaux, Bovée, and Claisse have called attention to the fact that complications may follow its use. In giving infusions the occurrence of acute cardiac dilatation must always be guarded against. When the pulse shows a large wave with but little resistance and a markedly slowed rhythm, great caution is necessary.

The following case is illustrative of the value of mechanical pressure. A cut-throat patient was admitted to the wards of Lakeside Hospital, exsanguinated and pulseless. Saline infusion and stimulants had been given in maximum amounts during twelve hours, but the circulation always relapsed, and at the time of the application of the rubber suit the pulse was barely perceptible, the respiration gasping, and the patient unconscious. On applying firm pneumatic pressure up to the costal borders the pulse became immediately better, the blood-pressure rising to 110 mm. of mercury, and consciousness was regained. The suit was worn for twelve hours, when the condition had sufficiently improved to warrant a gradual decompression. Recovery followed.

Another illustrative case was that of a delicate ten-year-old girl with very extensive tuberculous glands on both sides of the neck and extending into the thorax, which were first subjected to excision on one side and later on the other. In the course of the latter operation the glands were found to be firmly adherent and extended well down below the clavicle and

sternum. While separating with difficulty the last large gland with the forefinger, there was a large gush of arterial blood from a lacerated subclavian artery whose wall had become diseased from the closely adherent infected gland. The wound was at once firmly packed and a massive pyramid of gauze was applied under pressure. At the end of seven days the hemorrhage was renewed and the patient became quite exsanguinated. The bleeding was then temporarily controlled by pressure while preparation was made for ligating the innominate artery. A full therapeutic dose of morphin was given, the lower extremities and the abdomen were covered with heavy layers of cotton batting and firmly bandaged. After the morphin had reached the maximum effect she was cautiously anesthetized, an assistant giving simultaneously in the median vein a saline infusion at the rate of 3 c.c. per minute, and more rapidly during the rapid hemorrhage during the exposure of the artery. The innominate was then ligated, collateral circulation fully returned twelve hours later, and the child made a good recovery.

The **regulation of the posture** of the patient after acute hemorrhage is most important. By lowering the head the blood gravitates toward the heart. By reversing the position and lowering the feet, not only cerebral anemia may occur, but also sudden failure of the heart. With the former position once assumed the patient should be kept in it until the lost blood has been replaced by enough suitable fluid to insure avoidance of such accidents.

Firm **bandaging** of the legs and abdomen over heavy layers of cotton may be an effective aid toward maintaining the blood-pressure. Still more effective is the even and exactly regulable pressure of the pneumatic rubber suit.

The lowered temperature occurring in acute hemorrhage should be met by the use of **artificial heat** so applied as not

to disturb the patient or to interfere with the more important measures. It should always be remembered that the lowered vitality predisposes to the formation of burns from heating apparatus at a temperature which would ordinarily produce no such effect.

In profound hemorrhage in which the number of red cells are so greatly reduced as seriously to decrease the amount of oxygen carried to the vital centers, the administration of **oxygen** is a most effective aid. Indeed, there is a stage of hemorrhage characterized by such a degree of suboxidation that the arterial blood assumes a peculiar port-wine hue in which recovery is not possible without the freest inhalation of oxygen or the use of transfusion.

In regard to the use of **transfusion of blood** in treating acute hemorrhages, the question of the substitution of entire similar blood for the lost blood is discussed fully under Part II. To summarize the results of the experimental and clinical evidence here, it may be stated that transfused blood is much better retained in the blood-vessels of the recipient than saline solution, it has the oxygen-carrying properties of the lost blood, and under favorable conditions it should prove, and has proved, to be the ideal treatment for acute hemorrhage. As it actually replaces what is lost, it must of necessity be better than a substitute. As with saline solution, transfusion of too large an amount of blood will cause it to pass out of the vessels into the body cavities and parenchymatous organs, but the therapeutic result is obtained long before there is any danger of this occurring.

HEMORRHAGE IN OPERATIONS

In performing surgical operations it is always well to bear in mind in estimating the effect of hemorrhage on a strong subject that from 2 to 3 per cent of the body weight of blood

may be lost without materially changing the blood-pressure; that the blood-pressure is then maintained at the expense of an increased action of the vascular nervous mechanism; and that such a patient, despite the apparently good circulation, cannot withstand shock or other depressing factors as well as a patient having a similar blood-pressure but who has lost no blood. Therefore the conservation of the blood is of supreme importance.

It is a good rule to operate only in a dry field, picking up all vessels as they bleed, or if possible before they are severed, and eventually tying them. The tying is important, for while few vessels may bleed at the end of an operation when the blood-pressure is lowered, they may ooze later when the pressure returns to the normal level, or particularly if the patient happens to vomit, when marked increase in the venous pressure occurs. In amputations, resections, etc., the method of plain dissection has been employed in the past few years in most instances; that is to say, an amputation of the thigh is done by precisely the same methods of dissection as an amputation of the breast. It is true that with a tourniquet less blood is lost during the division of the tissues, but the total amount finally lost during the first twenty-four hours has certainly been lessened by applying the methods of plain dissection to these operations. In using the Esmarch tourniquet oozing continues for a considerable time after the operation has been completed. Postoperative oozing is poorly borne in the presence of shock.

In more serious operations of the neck, face, and head, a previously described method of temporarily closing the large arteries by means of a special clamp has been used by the author nearly one hundred times in controlling hemorrhage in patients whose ages ranged from nine months to seventy-nine years. No unfavorable results have been noted. The common carotid

artery is so readily exposed, provided one disregards the teaching of anatomists, and merely makes an intramuscular division of the sternomastoid muscle, that it adds but little to the operative technic. The closure of the artery does not entirely control even the arterial hemorrhage of the region supplied on account of the rich anastomosis of both the external and internal carotids. In elderly subjects, for example, with atheromatous blood-vessels and high blood-pressure, a distinct recurrent pulse has been seen in the branches of the external carotid artery when the common carotid was totally closed by the clamp. The opposite carotid supplied such a volume of blood under high tension to the brain that a pulse wave extended through the peripheral vessels in the brain back through the internal carotid, and then up the external carotid to its terminal branches, thus giving a pulsating circulation from the opposite side of the neck. This is, however, quite unusual in the author's experience.

The closure of both external carotids would naturally entirely control the arterial hemorrhage. This has been done by the author several times. It was found that the patients required but little anesthetic, and that the respiration was affected more than the circulation.

It has not been found that the closure of the common carotid artery is of any special advantage in those operations on the brain in which the principal risk of hemorrhage is from the venous circulation. In operating on the Gasserian ganglion it has been the author's custom to do so because it so much minimizes hemorrhage from dividing the massive soft tissues encountered in this operation, as well as that from the diploë and the coverings of the brain. With this stage of the operation once passed the closure no longer has any effect on the hemorrhage, because what then occurs is mostly of venous origin. The latter may be minimized greatly by the inclined

head-up posture, and the use of the rubber pneumatic suit to prevent resulting cerebral anemia.

Closure of the common carotid artery has been found to be particularly and even strikingly helpful in operating on aneurysms of the various parts of the scalp, skull, or orbit. Recently in operating on a large bulging tumor protruding through a previous osteoplastic opening in the skull the hemorrhage was better controlled by the application of a piece of thin rubber dam, such as dentists use, as a close-fitting turban through which the incision was made. This method has also been employed in securing a bloodless field in other operations on the skull.

In operations in the buccal cavity, such as for cleft palate, excision of the tongue, or of the jaw, etc., the method of giving the anesthetic is of great importance. The best method in the experience of the author is to give it by entubage of the pharynx through the nares. By this method, which has been previously described elsewhere, an even anesthesia may be maintained, not a drop of blood need be lost, the anesthetizer is out of the way of the operator, and the latter is as free to execute an exact technic as he would be in performing a herniotomy or other operation away from the head. Not only are obvious dangers and inconveniences obviated, but in case of cleft-palate operations, for example, a piece of gauze may be easily packed firmly against the palatine artery so as effectively to control the hemorrhage. In partial excision of the tongue the pharyngeal packing may be so arranged as practically to close the supplying arteries. Using this method in operations for cleft palate, the author has noted absence of fever and the other symptoms of sapremia which so often followed the old technic.

In operating on suitable cases of tumors of the neck the internal carotid artery is temporarily closed. In addition, if

there is an unusual risk of hemorrhage, the patient is incased in a rubber pneumatic suit and placed at an angle of 45°. Here, too, as mentioned above in referring to operating on the Gasserian ganglion, the upright posture diminishes the venous hemorrhage by allowing the blood to gravitate downward, while any tendency toward harmful cerebral anemia is controlled by inflating the suit to the right degree as needed. An observer need only to note the fading out of the color in the superficial blood-vessels as the body is elevated to appreciate how great the effect is in minimizing hemorrhage. In this way a dry operative field may be maintained without difficulty for the clean dissection of any portion of the neck.

PART II

TRANSFUSION

INTRODUCTION

In undertaking the study of the transfusion of blood the general plan has been to obtain a foundation for later work rather than to carry out any particular branch to a point where further investigation would seem useless. Many problems have arisen together, and the endeavor has been to do enough to assure the avoidance of the most likely pitfalls in connection with the clinical application of the results. The welfare of the patient should always be the first consideration, and it is hardly necessary to say that this fact has been the keynote throughout the clinical work.

The author feels satisfied that he has reduced the technic of the operation of transfusion to a sound basis. Mastery of the technic is not alone sufficient, however, as under the two general headings of the mechanics and the therapeutics of transfusion many facts are gathered which must be clearly understood before an adequate knowledge of the subject can be had. These facts are discussed in their appropriate places.

With our present knowledge the author distinctly feels that the direct transfusion of blood from one person to another should be done only as a last resort after all ordinary means of treatment have failed, or in cases which, from the outset, are known to be incurable. He is convinced that patients have been saved by its use who otherwise would surely have died, and on that account he feels justified in presenting the facts contained in these pages.

A word should be said in regard to the use of terms in

connection with transfusion. The words "donor" and "donee" have been used by English writers to designate the giver and the receiver of the blood respectively. While convenient on account of their brevity, it is found that their similarity may lead to confusion and even to error. For this reason the word "recipient" has been substituted for the word "donee," and is used in preference to it throughout this book.

According to the most recent standard dictionaries the word "transfusion" may mean the introduction of either saline solutions or blood into the vascular system of the recipient. To avoid confusion and to insure brevity the use of this word has been restricted to mean transfusion of blood, and is so used throughout.

CHAPTER VII

A BRIEF HISTORY OF TRANSFUSION

It is impossible to say when and where the idea first originated of transferring blood from an animal or a person to the veins of a person suffering from the loss of blood or afflicted with disease. That the ancient Egyptians knew about it and practiced it is probable from allusions made in their history. In the "Book of Wisdom" of Tanaquila, the wife of Tarquin, mention is made of the custom, and Herophilus clearly refers to it in his treatise on anatomy. In the sacred book of the priests of Apollo it is also referred to, and it is mentioned in the researches of Eubages, the works of Pliny and of Celsus, where it is condemned, and in the Metamorphoses of Ovid. At a much later time La Martinière, in writing to M. de Colbert, says that transfusion was experienced by Martel Ficin, Abbot Trithème, and Fra Paola.[1]

What is probably the earliest authentic case on record is that of Pope Innocent VIII, who was operated on in April, 1492. "The vital powers of Innocent VIII rapidly gave way; he had for some time fallen into a kind of somnolency, which was sometimes so profound that the whole court believed him to be dead. All means to awaken the exhausted vitality had been resorted to in vain, when a Jew doctor proposed to do so by the transfusion, by a new instrument, of the blood of a young person—an experiment which had hitherto only been

---

[1] Much of the material for this short historical account has been taken from Oré's excellent monograph.

made in animals. Accordingly, the blood of the decrepit old pontiff was passed into the veins of a youth, whose blood was transferred into those of the old man. The experiment was tried three times, and at the cost of the lives of three boys, probably from air getting into their veins, but without any effect to save that of the pope" (Villari's "Life of Savonarola"). This case, besides being the first authentic one, is the first in which death was ascribed to air embolism.

In 1615 transfusion is accurately described by Libavius without there being evidence that he practiced it. The author of a book entitled "Relatione de l'Expérience faite in Engleterra, Francia, etc.," cites the passage from Libavius and goes on to say that he did not propose it seriously, for on being questioned as to what should be done to prevent the donor of the blood from becoming weak, he replies that there is more need of protecting the physician who proposes the operation, and that while the former should have some good broth, the latter should be given hellebore! (Oré).

In 1628 Giovanni Colle, of Padua, in speaking of foods and medicines which would be likely to prolong life, mentions transfusion as a means of doing so.

Francesco Folli gave a reading before Ferdinand II of Tuscany in which his intention of performing transfusion was stated, and in 1652 he wrote the following: "I have read William Harvey's book, which treats of the movement of the heart and of the blood. This reading, with some ideas I had on the grafting of plants, gave rise in my mind to this third problem, that, the circulation of the blood existing, it would be possible to perform transfusion, by means of which one could not only cure but rejuvenate and make robust" (translated from Oré). Folli used two cannulas in performing transfusion—one of bone and the other of silver. They were connected by a piece of intestine or by a piece of prepared

artery, and there was a side branch which permitted the escape of air.

It was not until about the middle of the seventeenth century that transfusion began to have an established place in surgery. Harvey's discovery of the circulation of the blood stimulated research, first on animals and then man, and gave a reasonable basis on which to account for the successes which occurred. New ideas were originated, new apparatus was invented, and an era of marked progress was inaugurated. Workers in France, Germany, and England were particularly active at this time, and it is difficult or impossible to say to whom belonged the greatest credit.

In January, 1667, there appeared in the *Philosopher's Journal* an article by Richard Lower in which he gave the first complete detailed account of the method of performing transfusion. According to this method, the carotid artery of one dog was freed, and, by means of quills, connected to the lower end of the jugular vein of another dog. When the blood was allowed to pass over, the upper end of the jugular vein of the recipient was unligated so that, as it received the new blood, it lost an equal amount of its own blood, a balance being thus maintained between inflow and outflow. By this method the donor of the blood was allowed to die.

In the same year Denys, of Montpellier, wrote concerning experiments which he performed on animals. He followed Lower's method in a general way except that he did not withdraw enough blood from the donor to cause death. He also tried transfusion from three calves to three dogs with success in each case. In a letter to M. de Montmore he describes two transfusions which he made on patients. His idea was that "In practicing transfusion one can only imitate the example of nature, which, in order to nourish the fetus in the uterus of the mother, makes a continuous transfusion of the blood of

the mother into the body of the infant through the umbilical vein. In performing transfusion it is nothing else than nourishing by a shorter road than ordinary—that is to say, placing in the veins blood all made in place of taking food which only turns to blood after several changes" (Oré).

His first patient was a young man sixteen years old who was in a stupor following a fever which had lasted two months, and in the course of which he had been bled 20 times. Denys withdrew 3 ounces of his blood and transfused 9 ounces of arterial blood from a lamb. The result was a complete cure.

In the second case the transfusion was apparently performed purely for experimental purposes, as the subject was well and strong and received a consideration for permitting it. About 10 ounces of blood were removed from a vein and an equal amount transfused from a lamb. The man experienced an agreeable sense of warmth, but had no unpleasant sensations and no ill effects occurred. Encouraged by these two successes, Denys tried a third time. The patient was a man thirty-four years old who had had intermittent insanity for eight years. In a violent attack he escaped from his place of confinement 12 miles from Paris and arrived in the latter place naked. After he was placed in confinement again Denys, with the help of Emmeretz, transfused 5 or 6 ounces of blood from a calf, and as soon as he became calm a still larger quantity. These operations took place toward the end of 1667, and the patient did not have a return of his symptoms until January, 1668.

While transfusion had its advocates, it also had its opponents, and among the most powerful were the Faculty of Medicine of Paris, who did not recognize Harvey's discovery of the circulation of the blood, and who opposed any progress being made in medicine. They stooped to publishing anonymous pamphlets against Denys and Emmeretz, and were even accused of having bribed the widow of the above-mentioned

insane man (who had died under circumstances pointing to her having poisoned him shortly after a third transfusion was attempted) to falsely accuse them of having caused her husband's death. A complaint was made by Denys to the authorities, and after a review of the case it was ordered that the woman should appear in court in person for further examination, and also that "A l'avenir la transfusion ne pourrait être faite chez l'homme sans l'approbation d'un médecin de la Faculté de Paris" (Antoine Daubray, Chatelet, April 17, 1668). As a result of this decree interest in transfusion was discouraged, and it was almost forgotten by all but a few observers until early in the nineteenth century.

In 1683, at Frankfort-on-the-Oder, the surgeons Kaufman and Purman are said to have cured a leper by transfusing into his veins blood from a lamb (Oré).

In 1682 Ettenmuller, of Leipsic, recommended transfusion in fevers, scurvy, and hypochondriasis. He said that small amounts of blood should be injected at different times.

In 1714 Nuck gave the history of transfusion in his book entitled "Operationes et Experimenta Chirurgica," saying it should not be forbidden, but that it might be of great value in wounds followed by hemorrhage of considerable amount. He did not approve of using the blood of animals in transfusing to man.

In 1749 Cantwell, a member of the Faculty of Paris, was of the opinion that transfusion should not be forbidden in desperate cases, as it had previously occasionally proved to be of value. Apparently either opinion was changing in the Faculty or he alone possessed the courage of his convictions.

In 1783 Michel Rosa, professor and president of the Faculty of Medicine of Modena, made some experiments, and apparently proved (1) that the vessels of a normal living animal can receive much more blood than they contain without being

filled, (2) that the transfusion of blood of an animal of another species can be performed without danger to life, and (3) that the reanimation of an exsanguinated animal can be accomplished by the introduction of arterial blood from an animal of another species (" Lettere fisioligiche," Naples, 1783).

In 1792, in Cambridge, Harwood reanimated an exsanguinated dog before an audience by means of transfusion.

In the same year at Eye, in the county of Suffolk, where there was an epidemic of hydrophobia, Russell first bled a young boy who was afflicted with the disease, and then transfused into his veins the blood of two lambs. Recovery resulted.

In 1796 Darwin extolled transfusion of the blood of man, sheep, or donkey in putrid fever, scirrhous of the esophagus, or in cases where there were obstacles to the proper nutrition of the patient due to any cause.

The beginning of a new era was signalized by the work of Blundell in England. After witnessing the death of a woman from uterine hemorrhage, he came to the conclusion that her life might have been saved by transfusion. As it would have been difficult from the circumstances of the case to have employed the ordinarily used immediate method, he thought that in a similar case the blood could be injected from a syringe. Fearing, however, that the blood would be changed by coming in contact with the interior of the syringe, he performed experiments on dogs for the purpose of investigating this point.

In his first experiment (*Medico-Chirurgical Transactions*, 1818, ix, 56) he withdrew 8 ounces of blood from the femoral artery of a dog. Most alarming symptoms soon showed themselves—difficulty of breathing, convulsions, loss of sensibility, and complete relaxation of the abdominal muscles. After some seconds 6 ounces of blood were taken from another dog and injected into the femoral vein, with the result that recovery

was complete. From this Blundell concluded that the use of the syringe did not affect the blood.

In his second experiment, tubes were introduced into the femoral vein and femoral artery of a dog, and as the blood escaped from the latter into a vessel it was at once injected into the former. This was continued for twenty-four minutes without the animal suffering any harm.

Blundell also tried other experiments to determine the effect of leaving the blood in the vessel a longer time, and of the effect of using dissimilar blood. He injected human blood into dogs after it had stayed in a vessel from thirty to sixty seconds, and found that they all died either immediately or in several days. He came to the conclusion that if air in not too large amount were injected into the veins the animal did not die. He found that venous human blood did not act better than arterial human blood in reanimating dogs after bleeding them. In particular he noticed that a much less amount of blood was necessary to reanimate a bled dog than the amount of blood lost by the dog.

In 1825 Prevost and Dumas said that: "If one takes the blood which one injects from an animal of different species, but whose corpuscles may be of the same shape although of different dimensions, the animal is only imperfectly bettered, and can rarely be saved more than six days. . . . If one injects blood with circular corpuscles into a bird, the animal ordinarily dies in the very midst of violent nervous manifestations comparable to those caused by the strongest poisons" (Oré).

About ten years later Bischoff began a series of experiments in which he tried the effect of transfusing defibrinated blood from mammals into birds, and repeated, using whole blood. He also tried to ascertain whether exsanguinated animals could be reanimated by transfusing blood from an animal of another species. He concluded that defibrinated mammalian blood did not exercise a deleterious influence on birds,

while if not defibrinated it caused death, and that defibrinated similar blood would not reanimate exsanguinated animals. He also concluded that the fibrin contained a harmful substance which was the immediate cause of death. In 1838 he has an account of further experiments in Müller's *Archives* (page 351) and concludes that the arterial blood of a mammal does not cause death when it is introduced into the veins of a bird, and that only venous blood leads to a fatal termination.

In 1875 Guérin tried connecting the arteries of two dogs so that their blood would circulate in common. He joined the central end of the severed femoral artery of Dog No. 1 with the peripheral end of the severed femoral artery of Dog No. 2 by means of a short rubber tube. Then he connected the peripheral end of the artery of Dog No. 1 with the central end of the artery of Dog No. 2 in the same way.

This gave a continuity of blood path which could rarely be maintained more than half an hour without clotting in the tubes. On trying the experiment on two horses the relation could apparently have been maintained indefinitely without clotting, but as the smaller horse became so plethoric that blood oozed from the intestinal mucous membranes the experiment was stopped. Beyond this oozing no other harm resulted. There is no record of this method ever having been tried on human beings.

EXPERIMENTAL STUDIES

CHAPTER VIII

TRANSFUSION FOR HEMORRHAGE, SHOCK, AND COMBINED HEMORRHAGE AND SHOCK

In collaboration with Drs. D. H. Dolley, F. W. Hitchings, C. H. Lenhart, and A. S. Eisenbrey.

PROTOCOLS OF EXPERIMENTS

Hemorrhage

EXPERIMENT 1

Hemorrhage

Bleeding from Dog B; Transfusion from Dog A to Dog B; After Five Days' Bleeding from Dog A; Transfusion from Dog B to Dog A; No Apparent Development of Antibodies in the Blood of Either Dog.

September 14, 1906.

Donor.—Yellow mongrel dog; weight, 10.6 kilos; condition, good. *Recipient.*—Black mongrel bitch; weight, 10.8 kilos; condition, good. Previous to the operation each dog was given $\frac{1}{4}$ grain of morphin. Ether anesthesia. The proximal end of the left carotid artery of the donor was sutured by Carrel's method to the distal end of the left carotid artery of the recipient. The femoral artery of the recipient was exposed. The operation was performed under asepsis. The blood-pressure was not recorded in this experiment. All data refer to the recipient, unless otherwise specified.

12.51.—Began to bleed from the femoral artery. The blood-pressure was strong.

1.00.—Stopped the bleeding. 350 c.c. blood removed. Began to transfuse.

1.08.—Double beats were obtained in the anastomosed carotids, indicating that the pressure in the vessels of the recipient was about the same as in the vessels of the donor.

1.10.—Stopped the transfusion; duration, ten minutes. The vessels were tied off and the wounds were dressed.

The recipient began to have general tremors before the operation was over. These soon developed into a severe chill, which lasted about four hours. It was impossible to say whether this was due to the transfusion or not, but no other unusual symptoms developed.

The blood counts before the transfusion were as follows:

Donor, Dog A.—Red corpuscles, 6,496,000; hemoglobin, 95 per cent; white corpuscles, 14,600.

Recipient, Dog B.—Red corpuscles, 4,960,000; hemoglobin, 100 per cent; white corpuscles, 16,200.

September 15, 1906.

Both dogs were in excellent condition. The donor was a little more lively than the recipient, and the latter had a slight hematoma in the neck incision, which was removed by loosening a stitch.

September 19, 1906.

Donor.—Weight, 10.8 kilos; condition, good. *Recipient.*—Weight, 9.2 kilos; condition, good. The object of the remainder of the experiment was to transfuse over again, but to transfuse back from the recipient to the donor. From this point on the dogs will still be designated as donor and recipient, but the terms will be changed according to the second transfusion. Hence, it must be remembered that the donor now was the recipient of the first transfusion, and the recipient the former donor. The anesthetics were the same as before —morphin and ether. Under asepsis the femoral artery of the donor was anastomosed to the femoral artery of the recipient by Carrel's method. All data refer to the recipient, unless otherwise specified.

12.42.—Began the transfusion.

12.50.—Stopped the transfusion. Duration, eight minutes.

12.52.—Began to bleed from the left femoral artery.

12.56.—Stopped the bleeding. 150 c.c. blood removed.

12.58.—Began to transfuse again.

1.05.—Stopped the transfusion; duration, seven minutes. Total duration, fifteen minutes.

1.40.—The recipient had a moderate chill.

1.53.—The chill had diminished very much. The vessels were tied off and the wounds were dressed.

The further blood counts and examinations were as follows:

1. Before the second transfusion: Recipient, Dog A.—Red corpuscles, 5,600,000; hemoglobin, 100 per cent; white corpuscles, 9,400. The fresh blood was normal in appearance. Donor, Dog B.—Red corpuscles, 6,240,000; hemoglobin, 100 per cent; white corpuscles, 9,800. The fresh blood was normal in appearance.

2. Five minutes after the transfusion: Recipient, Dog A.—The fresh blood was normal in appearance.

3. Twenty-five minutes after the transfusion: Recipient, Dog A.—The fresh blood was normal in appearance.

4. Fifty-five minutes after the transfusion: Recipient, Dog A.—The fresh blood was normal in appearance.

5. Four and one half hours after the transfusion: Recipient, Dog A.—The fresh blood was normal in appearance.

6. Twenty-four hours after the transfusion: Recipient, Dog A.—Red corpuscles, 6,400,000; hemoglobin, 100 per cent; white corpuscles, 9,000.

Summary.—The transfusion from Dog A to Dog B, and the retransfusion in five days from Dog B to Dog A, did not result in the formation of antibodies at either time with changes which were appreciable by examination of the blood as carried out in the experiment, nor was their presence indicated by the appearance of untoward symptoms. Transfusion served as an ideal treatment for hemorrhage in each instance.

EXPERIMENT 2

Hemorrhage

Bleeding from Dog A; Transfusion from Dog B; Second Bleeding from Dog A after Elapse of Ten Days; Retransfusion from Dog B; No Apparent Development of Antibodies in Blood of Dog A.

September 15, 1906.

Donor.—Slim-bodied mongrel dog; weight, 12.4 kilos; condition, good. *Recipient.*—Mongrel bitch; weight, 5.5 kilos; condition, good, although an old dog. Before the operation each dog was given ¼ grain of morphin. Ether anesthesia. Under aseptic conditions the left carotid artery of the donor was anastomosed to the left carotid artery of the recipient by Carrel's method. At first there was slight oozing on testing the anastomosis, but this soon stopped. The femoral artery of the recipient was exposed. The blood-pressure was not recorded on the drum. All data refer to the recipient, unless otherwise specified.

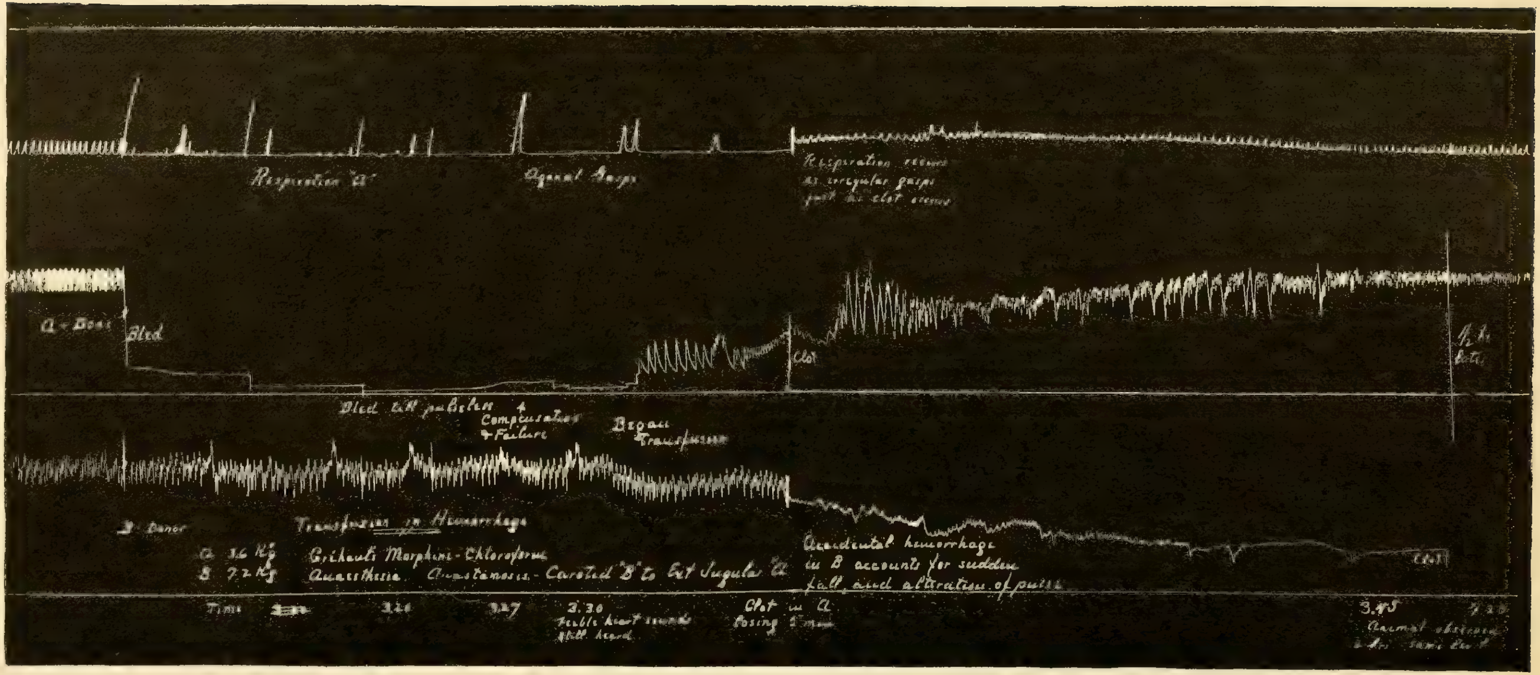


FIG. 26.—TRANSFUSION AFTER COMPLETE EXSANGUINATION (RESPIRATORY, THOUGH NOT CARDIAC, FAILURE OCCURRED) RESTORED THE DOG, AND STEADILY MAINTAINED THE BLOOD-PRESSURE DURING AN OBSERVATION OF TWO AND ONE HALF HOURS.

11.33.—Began to bleed the recipient from the femoral artery.

11.40.—Stopped the bleeding, 240 c.c. being removed. The respirations were very slow and there was no pulsation of the carotid artery where it was exposed. The mucous membranes were very pale.

11.41.—The respirations almost ceased. The transfusion was begun, and allowed to proceed slowly.

11.41½.—The breathing was less shallow and gradually improving. The blood-pressure in the donor was not very strong.

11.48.—There was a double pulsation in the anastomosed vessels. The transfusion was stopped; duration, seven minutes. The color of the mucous membranes was much improved. The wounds were dressed.

12.35.—The recipient had a slight chill.

The blood counts before the operation were as follows:

Donor.—Red corpuscles, 7,680,000; hemoglobin, 100 per cent; white corpuscles, 24,000.

Recipient.—Red corpuscles, 6,976,000; hemoglobin, 100 per cent; white corpuscles, 20,000.

September 17, 1906.

Both dogs were lively and in excellent condition after the lapse of forty-eight hours. No untoward symptoms were shown at any time.

September 25, 1906. Retransfusion.

Donor.—Weight, 11.3 kilos; condition, good. *Recipient.*—Weight, 5.4 kilos; condition, good. The object was to retransfuse exactly as before without changing the donor and the recipient. Each dog was given ¼ grain of morphin before the operation. Ether anesthesia. Under aseptic conditions the right external carotid artery of the donor was anastomosed to the left femoral vein of the recipient by Carrel's method. It was found that the donor's right external carotid artery and external jugular vein were very much dilated owing to the increased pressure caused by tying off the left carotid artery ten days previously. All data refer to the recipient, unless otherwise specified.

11.40.—Began to transfuse slowly.

11.41.—The blood was allowed to pass over more rapidly.

11.47.—Stopped the transfusion; duration, seven minutes. The respirations, which had been very shallow during the entire experiment up to this time, became stronger. The donor's remaining common carotid artery was tied off.

12.10.—The wounds were sewed up and dressed and the dogs were put to bed. On lifting the recipient from the operating table she immediately had violent convulsive movements. The front legs were crossed firmly on the chest, the head was drawn as far as possible to the right side of the body, the right pupil seemed to be of normal size, and the left pupil was dilated. The respirations were rapid and gasping, as if there were difficulty in inspiring. There was a slight hemorrhage from the left nostril. It was believed that these symptoms were due to overloading the circulation because the preliminary bleeding was omitted. On weighing the recipient she was found to have gained 0.22 kilo. The abdomen was rigid and tympanitic. There was no opisthotonos. The knee jerks and other tendon reflexes could not be obtained owing to the rapid movements of the extremities. On turning the recipient over to the other side the head fell toward that side somewhat, but was not drawn around as it was to the right.

12.22.—Respirations, 44 per minute. The heart beat was rapid and weak.

12.24.—The abdomen was still markedly distended and tense.

12.27.—The convulsive movements were less violent. The fresh blood was examined.

12.30.—The inspirations were still labored.

12.42.—The symptoms were much abated.

The blood counts and examinations were as follows:

1. Before the (second) transfusion: Recipient.—Red corpuscles, 3,964,000; hemoglobin, 75 per cent; white corpuscles, 20,000. The fresh blood was normal in appearance.

2. After the transfusion: Recipient.—The fresh blood was normal in appearance both during and after the convulsion.

September 26, 1906.

Both dogs were lively and apparently in excellent condition. The donor seemed to be none the worse for having his second carotid artery tied off. His pupils were equal. The recipient's abdomen was slightly firm, but it was not tender or distended. Her pupils were of equal size. The examination of her fresh blood showed nothing abnormal.

Summary.—The blood examinations in this experiment were negative as far as they were carried. After the second transfusion the recipient apparently suffered from acute dilatation of the heart with transudation of blood into the abdominal cavity, but was only temporarily inconvenienced. The transfusion served as an ideal treatment in replacing the lost blood in each case.

EXPERIMENT 3

Shock; Transfusion

Donor.—White spaniel; weight, 7.2 kilos; condition, good. *Recipient.*—Black mongrel; weight, 5.4 kilos; condition, good. Ether anesthesia. The carotid artery of the donor was anastomosed to the internal jugular vein of the recipient by Carrel's method. The carotid blood-pressure of both dogs was recorded on a drum. The initial blood-pressure of the donor was 140 mm., and of the recipient 130 mm. At first the larynx and trachea of the recipient were manipulated, and then the production of shock was attempted in the usual manner by manipulating the intestines, burning the paws, etc. This was done for nearly one and one half hours, when the following records were made:

12.40.—Control on drum. The recipient was in moderate shock, with the reflexes not entirely gone. Blood-pressure of the recipient, 50 mm. Blood-pressure of the donor, 116 mm. Transfusion was begun, and the flow was rather rapid at first.

1.00.—Stopped the transfusion. Recipient.—Blood-pressure back to the initial level of 130 mm. The height of the pulse wave was somewhat diminished. Donor.—Blood-pressure, 27 mm.

3.00.—Control. Recipient.—Blood-pressure, 118 mm., a fall of 12 mm. in one hour and fifty-nine minutes. As the experiment could not be carried any further, the recipient was killed. (The donor was killed some time previously.)

Summary.—After a transfusion of twenty minutes the blood-pressure of a dog which had been reduced 80 mm. through shock was brought back to the original level, and remained within 12 mm. of the original level for almost two hours.

EXPERIMENT 4

Shock; Transfusion

Donor.—Dog; weight, 7.2 kilos; condition, good. *Recipient.*—Dog; weight, 5.4 kilos; condition, poor. Ether anesthesia. The carotid artery of the donor was anastomosed to the internal jugular vein of the recipient by Carrel's method. The carotid pressure of both dogs was recorded on a drum. The initial blood-pressure of the donor was 110 mm., and of the recipient 96 mm.

10.30–12.13.—Shock was produced in the recipient by the usual methods.

12.13.—Control on drum. Recipient.—Blood-pressure, 28 mm. Burning a paw gave a very slight reaction the first time, and no reaction the second time. Cardiac failure appeared imminent.

12.15.—The transfusion was begun gradually. Recipient.—The blood-pressure immediately rose with the transfusion, and the heart beats, which at first were very irregular, showed after a little an occasional approach to a normal rhythm. This became more frequent, and at about 12.25 the heart tone was normal, the pressure had risen to 70 mm., and the stroke was nearly that at the beginning of the experiment. The maximum blood-pressure was reached in about eight minutes.

1.00.—Stopped the transfusion.

1.01.—Stopped the drum. A clot was present in the carotid cannula of the recipient, and this was partly removed then, and completely removed four minutes later. Blood-pressure, 68 mm. At this point the blood-pressure of the donor was down to 12 mm., and cardiac failure was beginning.

2.00.—Control. Recipient.—Blood-pressure, 50 mm. The length of the heart stroke was diminished by one half.

3.15.—Control. Recipient.—Blood-pressure, 22 mm. Cardiac failure was beginning. The previous pressure reached was maintained definitely for nearly fifty minutes. After forty-five minutes more the pressure fell to 18 mm. During the next one and a quarter hours the pressure fell to the danger level with beginning cardiac failure. After the production of shock the abdomen was closed and no post-mortem examination was made.

Summary.—After slow transfusion for forty-five minutes the blood-pressure of a dog in previously poor condition which had been reduced from 96 mm. to 68 mm. through shock, was brought back to 70 mm. (within 26 mm. of the original point), and maintained for fifty minutes before it began slowly to fall.

EXPERIMENT 5

Shock; Transfusion

Donor.—Bull terrier; weight, 17.2 kilos; condition, good. *Recipient.*—Mongrel; weight, 8.1 kilos; condition, good. Chloroform-morphin anesthesia. The carotid artery of the donor was anastomosed to the femoral vein of the recipient by Carrel's method. The carotid pressure of both dogs was recorded on a drum.

11.20.—Control. Donor.—Blood-pressure, 126 mm. Recipient.—Blood-pressure, 110 mm.

11.40.—Control. Blood-pressure the same for both dogs.

12.00.—Control. Donor.—Blood-pressure, 130 mm. Recipient.—Blood-pressure, 140 mm. Burning a paw was followed by a sharp rise of pressure from a falling level.

12.05.—Recipient.—Began to produce shock, principally by opening the abdomen and manipulating the intestines.

1.40.—Control. Donor.—Blood-pressure, 112 mm. Recipient.—Blood-pressure, 31 mm.

1.48.—Control. Recipient.—Cardiac failure began. On burning a paw there was a slight reaction. There was complete respiratory failure, and artificial respiration was begun.

1.56.—Recipient.—After a prolonged burning of a paw there was no reaction.

2.00.—Donor.—Blood-pressure, 110 mm. Recipient.—Blood-pressure, 28 mm. On burning a paw there was no reaction.

2.01.—Started the transfusion.

2.04.—Stopped the transfusion. Donor.—Blood-pressure, 90 mm. Recipient.—Blood-pressure, 72 mm.

2.06.—Control. Recipient.—Spontaneous respiration began. Began to transfuse again at about this time.

2.13.—Stopped the transfusion temporarily. Recipient.—Blood-pressure, 110 mm. The heart action was irregular. A clot was removed from the carotid cannula.

2.15.—Started the drum and the transfusion.

2.20.—Stopped the drum and the transfusion. Donor.—Blood-pressure, 11 mm. Recipient.—Blood-pressure, 114 mm. The maximum level of the pressure was reached fifteen minutes after the transfusion was begun, but the pressure then began to fall within three minutes.

2.25.—Control. Donor.—Blood-pressure, 6 mm. Recipient.—Blood-pressure, 105 mm.

2.30.—Recipient.—The blood-pressure was falling rapidly. On opening the abdomen a moderate amount of blood was found which had apparently issued from slight mesenteric tears caused in producing shock.

2.35.—Control. Recipient.—Blood-pressure, 68 mm. There were approximately 100 c.c. of blood in the abdominal cavity.

2.40.—Recipient.—On burning a paw there was scarcely an appreciable reaction. The respiration began to fail.

2.45.—Control. Recipient.—Blood-pressure, 55 mm.

3.00.—Control. Blood-pressure, 54 mm.

3.20.—Control. Recipient.—Blood-pressure, 47 mm.

4.00.—Control. Recipient.—Blood-pressure, 20 mm. About 200 c.c. of blood were found in the abdominal cavity.

Note.—At the time this experiment was performed the hemorrhage into the abdominal cavity, which was a direct cause of the immediate fall of the blood-pressure, was attributed to the injury done in the manipulation in producing shock, although only a few minute tears in the mesentery were found. In the light of later experiments it is probable that this hemorrhage was largely due to a transudation of blood.

Summary.—After a transfusion of about fifteen minutes' duration, the blood-pressure of a dog which had been reduced 112 mm. through shock was brought back 86 mm., the maximum level being reached fifteen minutes after the transfusion was begun. Owing to the transudation of blood into the abdominal cavity (due to excessive transfusion) the pressure was not maintained.

EXPERIMENT 6

Shock; Transfusion

Donor.—Bull terrier; weight, 15.8 kilos; condition, good. *Recipient.*—Mongrel; weight, 9.9 kilos; condition, good. Chloroform-morphin anesthesia. The carotid artery of the donor was anastomosed to the femoral vein of the recipient by Carrel's method. The carotid pressure of both dogs was recorded in the usual way.

11.20.—Control on drum. Donor.—Blood-pressure, 90 mm. Recipient.—Blood-pressure, 72 mm.

11.25.—Control. Recipient.—On burning a paw there was a rise of pressure of 4 mm. at first, followed by a sharp rise of 10 mm. more to 86 mm.

11.27.—Control. Recipient.—On burning a paw there was a sharp rise of pressure of 10 mm.

11.30.—Control. Recipient.—The same reaction was obtained on burning the paw.

11.35.—Control. Recipient.—Blood-pressure, 86 mm. Began to produce shock.

12.30.—Control. Recipient.—The blood-pressure was reduced to 30 mm.

1.10.—Control. Recipient.—On burning a paw there was no change in the blood-pressure.

1.15.—Began to transfuse.

1.19.—Recipient.—Blood-pressure, 40 mm.

1.23.—Control. Recipient.—Blood-pressure, 42 mm.

1.28.—Recipient.—Blood-pressure, 50 mm.

1.38.—Recipient.—Blood-pressure, 70 mm. The maximum pressure was obtained thirty-seven minutes after starting the transfusion, and at once began to fall. Donor.—Blood-pressure, 60 mm.

1.40.—Stopped the drum and the transfusion. Recipient.—It was found that hemorrhage was occurring from several lobes of the liver. An attempt made to stop it by cauterizing and ligaturing was only partially successful. Up to 1.50 there was a fall of pressure of over 20 mm. while the effort was made to stop the hemorrhage. Transfusion was begun again, but the rise in pressure was only temporary.

2.00.—Control. Blood-pressure, 44 mm.

2.20.—Control. Blood-pressure, 26 mm. It was impossible to control the hemorrhage and the dog quickly died.

Note.—The same remarks apply to this experiment as to the last one. Here again at the time of the experiment the hemorrhage was considered to be due to the manipulation, but it does not seem probable that this could have caused such extensive ruptures as were present, especially as they were chiefly on the under surface of the liver.

Summary.—After a transfusion of twenty-five minutes the blood-pressure of a dog which had been reduced 42 mm. through shock was brought back 40 mm., the maximum level being reached thirty-seven minutes after the transfusion was begun. Transudation of blood into the abdominal cavity from the liver occurred, and the blood-pressure was not maintained.

EXPERIMENT 7

Shock; Transfusion

Donor.—Bull terrier; weight, 11.7 kilos; condition, good. *Recipient.*—Mongrel skye terrier; weight, 8.1 kilos; condition, good. Chloroform-morphin anesthesia. The carotid artery of the donor was anastomosed to the external jugular vein of the recipient by Carrel's method. The carotid pressure of both dogs was recorded in the usual way.

11.20.—Donor.—Blood-pressure, 126 mm. Recipient.—Blood-pressure, 120 mm.

11.25.—Control. Recipient.—On burning a paw there was a rise of pressure of over 30 mm., and this level was maintained. Shock

was produced by opening the abdominal cavity and pulling out some of the coils of intestines in order to manipulate them without introducing the hand into the abdominal cavity. The coils were handled carefully to avoid traumatism.

1.00.—Control. Recipient.—Blood-pressure, 40 mm. On burning a paw there was a slight reaction. The production of shock was continued.

1.50.—Control. Recipient.—On burning a paw there was no reaction.

1.51.—Began to transfuse, at first rather rapidly and without good control of the flow. Recipient.—The blood-pressure rose to 114 mm. in three minutes and the heart was greatly overtaxed. The latter partly recovered after slowing the rate of transfusion, and showed complete recovery inside of four minutes, although the pressure had then fallen to 72 mm.

1.56.—Stopped the drum and the transfusion.

2.00.—Control. Recipient.—Blood-pressure, 72 mm.

2.10.—Recipient.—Blood-pressure, 66 mm.

2.13.—Recipient.—The pressure was the same. At this point the abdominal cavity, which had heretofore been kept closed, was opened, and considerable hemorrhage was found. Transudation of blood from the mesentery occurred while the latter was being observed.

2.30.—Control. Recipient.—Blood-pressure, 34 mm.

2.50.—Control. Recipient.—Blood-pressure, 30 mm. The dog was killed.

Summary.—After a transfusion of five minutes the blood-pressure of a dog which had been reduced 80 mm. through shock was brought back 74 mm., with the heart becoming greatly overtaxed, but with speedy recovery. The subsequent fall in pressure was rapid, and apparently associated with the transudation of blood into the abdominal cavity.

EXPERIMENT 8

Shock; Transfusion

Donor.—Mongrel collie; weight, 10.4 kilos; condition, good. *Recipient.*—Fox terrier; weight, 8.1 kilos; condition, good. Chloroform-morphin anesthesia. The carotid artery of the donor was anastomosed to the external jugular vein of the recipient. The carotid pressure of both dogs was recorded in the usual way.

10.30.—Donor.—Blood-pressure, 100 mm. Recipient.—Blood-pressure, 80 mm.

10.35.—Control. Recipient.—On burning a paw there was a rise of pressure of 24 mm.

10.45.—Recipient.—Began to produce shock by burning. The abdominal cavity was not opened.

10.55.—Control. Recipient.—Blood-pressure, 110 mm. Donor.—Blood-pressure, 112 mm.

11.37.—Recipient.—Blood-pressure, 35 mm. The heart showed signs of failure—the beats were very slow and arrhythmic.

11.41.—Recipient.—On burning a paw there was moderate reaction of the blood-pressure.

11.42.—Recipient.—On burning a paw there was no reaction. Blood-pressure, 30 mm. Donor.—Blood-pressure, 106 mm.

11.43.—Began to transfuse.

11.50.—Recipient.—Blood-pressure, 58 mm. The height of the pulse wave was equal to the initial height. Donor.—Blood-pressure, 64 mm.

11.55.—Control. Recipient.—Blood-pressure, 80 mm.

11.59.—Recipient.—Blood-pressure, 90 mm. This was the maximum height reached after the transfusion, and was maintained for eight minutes.

12.05.—Recipient.—On burning a paw there was a moderate reaction. A few spontaneous respirations were noted.

12.10.—Stopped the transfusion. Recipient.—Blood-pressure, 90 mm. The length of the heart stroke gradually diminished.

12.15.—Control. Recipient.—The blood-pressure fell steadily for the next ten minutes.

12.20.—Recipient.—Stopped the artificial respiration. Stimulation of the anus produced spontaneous respiration.

1.00.—Control. Recipient.—Cardiac failure was imminent. Blood-pressure, 22 mm.

1.05.—Control. Recipient.—Blood-pressure the same. Artificial respiration had no effect.

Autopsy.—From 350 to 400 c.c. of clotted blood were found in the abdominal cavity. The liver showed no signs of being ruptured. The intestinal walls were very congested and boggy. The thoracic cavity was perfectly clear.

Summary.—After a transfusion of twenty-three minutes the blood-pressure of a dog which had been reduced 50 mm. through shock, with the heart showing signs of failure, was brought back 60 mm., with return of the heart to its previous condition. The subsequent fall in pressure was gradual, and was apparently associated with transudation of blood into the abdominal cavity.

EXPERIMENT 9

Shock; Transfusion

Donor.—Mongrel dog; weight, 12.2 kilos; condition, good. *Recipient.*—Mongrel fox terrier; weight, 7.2 kilos; condition, good. Chloroform-morphin anesthesia. The carotid artery of the donor was anastomosed to the external jugular vein of the recipient by Carrel's method. The carotid pressure of both dogs was recorded in the usual way.

11.00.—Donor.—Blood-pressure, 126 mm. Recipient.—Blood-pressure, 98 mm. On burning a paw there was a rise in pressure of 30 mm., which was followed by a secondary rise, the latter being maintained.

11.05.—Control. Donor.—Blood-pressure, 138 mm. Recipient.—Blood-pressure, 126 to 132 mm.

11.15.—Control. Recipient.—Blood-pressure, 110 mm. Began to produce shock by burning.

11.20.—Control.

11.25.—Control. Recipient.—Blood-pressure, 50 mm. The reflexes were not tested.

11.54.—Control. Recipient.—Blood-pressure, 40 mm. The transfusion was begun at a rather rapid rate.

11.56.—Stopped the drum.

12.05.—Control. Recipient.—The blood-pressure at the end of the transfusion was raised 12 mm. above what it was just before the transfusion. The maximum level was obtained in eleven minutes, and during this time the blood-pressure of the donor fell from 120 mm. to 46 mm., which with rapid bleeding would mean a loss of one fifth to one fourth of its blood.

Autopsy.—The abdomen was distended, and on opening it numerous hemorrhages were found, which were due to multiple ruptures of the liver, particularly on its inferior surface, and also between several of the lobes. There were also small hemorrhages in the mesentery.

Summary.—After transfusion the blood-pressure of a dog which had been reduced 70 mm. through shock, with the heart showing signs of failure, was brought back 82 mm. As the experiment was then discontinued, no observation was made as to the time that the pressure was maintained, but as transudation of blood had occurred into the abdominal cavity it would probably have begun to fall very soon.

COMPARISON OF TRANSFUSION AND SALINE INFUSION IN THE TREATMENT OF SHOCK

EXPERIMENT 10

Shock; Intravenous Saline Infusion; Transfusion

NOVEMBER 7, 1906.

Donor.—Black and white mongrel dog; condition, good. *Recipient.*—Black mongrel puppy bitch; weight, 3.3 kilos; condition, good. Ether anesthesia for both dogs through tracheal cannulæ. The carotid artery of the donor was anastomosed to the femoral vein of the recipient by the Carrel method. The blood-pressure of the recipient was recorded in the usual way. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	11.20	124 mm.	Began to produce shock.
2	11.29	110 mm.	
3	11.31	94 mm.	
4	12.41	84 mm.	
5	12.54	80 mm.	
6	1.03	72 mm.	
7	1.11	60 mm.	
8	1.40	54 mm.	
9	2.04	48 mm.	
10	2.26	42 mm.	
11	2.29	38 mm.	
12	2.45	33 mm.	
13	2.53	36 mm.	
14	3.02	36 mm.	
15	3.03	40 mm.	Began to inject normal saline solution via the femoral vein.
16	3.05	36 mm.	
17	3.10	40 mm.	
18	3.12	42 mm.	
19	3.13½	42 mm.	
20	3.19	40 mm.	Stopped injecting saline solution. Total amount given, 300 c.c. The average head of pressure was 3 feet.
21	3.21	42 mm.	
22	3.30	40 mm.	
23	3.40	40 mm.	
24	3.45	58 mm.	Began the transfusion.
25	3.47	60 mm.	The transfusion was stopped for a few seconds on account of the appearance of symptoms indicating acute dilatation of the heart. Subsequently the anastomosed vessels were constricted so as to have the flow equal that of the former saline flow as nearly as possible.

Control	Time	Blood-Pressure	Remarks
26	3.50	74 mm.	
27	3.51	86 mm.	
28	3.52	98 mm.	
29	3.53	102 mm.	Stopped the transfusion. Duration, eight minutes.
30	3.55	96 mm.	
31	4.00	86 mm.	
32	4.15	84 mm.	
33	4.30	80 mm.	
34	4.45	86 mm.	
35	5.00	70 mm.	
36	5.15	60 mm.	
37	5.33	56 mm.	The dogs were killed. The respirations were at the rate of 36 per minute. The reflexes were normal, and the general condition was good.

Summary.—The blood-pressure of the recipient was reduced 88 mm. by shock. On injecting 300 c.c. of normal saline solution intravenously the pressure was unaffected. After transfusing for eight minutes it was raised a maximum of 62 mm. After this it slowly fell to 46 mm. in one hour and thirty-eight minutes, when the dog was killed.

EXPERIMENT II

Shock; Intended Intravenous Saline Infusion; Transfusion

November 15, 1906.

Donor.—Black mongrel bitch; weight, 9.5 kilos; condition, good. *Recipient.*—Brown mongrel dog; weight, 7.2 kilos; condition, good. Ether anesthesia for both dogs through tracheal cannulæ. The carotid artery of the donor was anastomosed to a femoral vein of the recipient by Carrel's method. The blood-pressure of the recipient was recorded on the drum. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	9.15	146 mm.	Began to produce shock.
2	9.24	136 mm.	
3	9.42	110 mm.	
4	10.13	94 mm.	
5	10.25	70 mm.	

Control	Time	Blood-Pressure	Remarks
6	10.36	62 mm.	
7	12.17	62 mm.	
8	12.27	56 mm.	
9	12.37	52 mm.	
10	1.00	48 mm.	
11	1.33	16 mm.	
12	1.35		"Death" occurred. The heart stopped beating, and the respirations ceased entirely. External massage of the heart and artificial respiration were begun, and maintained for twenty minutes. Began to transfuse.
13	1.44	56 mm.	The respiration and circulation were re-established.
14	1.47	66 mm.	
15	1.52	76 mm.	A clot was removed from the anastomosed vessels. The transfusion was stopped. Duration about seventeen minutes.
16	1.56	100 mm.	
17	1.58	110 mm.	
18	2.15	120 mm.	
19	2.30	122 mm.	
20	2.47	130 mm.	
21	3.00	140 mm.	
22	3.15	143 mm.	
23	3.30	143 mm.	
24	3.47	140 mm.	
25	4.05	134 mm.	
26	4.17	134 mm.	
27	4.30	130 mm.	
28	4.45	130 mm.	
29	5.04	126 mm.	
30	5.15	124 mm.	The dogs were killed.

NOTE.—The original intention was to try the effect of the intravenous injection of normal saline solution before beginning the transfusion, but owing to the "death" of the dog, this could not be done.

Summary.—After the complete cessation of the respiration and circulation, and the reduction of the blood-pressure to zero, artificial respiration and manipulation of the heart were performed at the same time that transfusion was begun, with a rise of the blood-pressure to 76 mm. at the end of the transfusion, and the resumption of the respiration and circulation. One hour and eight minutes after the transfusion the pressure had risen to 140 mm., and was maintained between 140 and 143 mm. for forty-seven minutes, when it began slowly to fall. When the recipient was killed at the end of three hours and twenty-three minutes after the transfusion the pressure was 124 mm.

EXPERIMENT 12

Shock; Intravenous Saline Infusion; Transfusion

NOVEMBER 16, 1906.

Donor.—Black and white mongrel bitch; weight, 7.2 kilos; condition, good. *Recipient.*—White mongrel bitch; weight, 6.3 kilos; condition, good. Ether anesthesia. The carotid artery of the donor was anastomosed to the femoral vein of the recipient by Carrel's method. The blood-pressure of the recipient was recorded on the drum. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	9.45	144 mm.	Began to produce shock by the usual methods.
2	10.00	84 mm.	
3	10.30	75 mm.	
4	1.04	76 mm.	
5	1.07	74 mm.	
6	1.20	70 mm.	
7	1.33	68 mm.	
8	1.35	58 mm.	
9	2.10	54 mm.	
10	2.27	52 mm.	
11	3.00	43 mm.	
12	3.55	36 mm.	
13	4.07	32 mm.	Stopped producing shock.
14	4.10	34 mm.	Began to inject normal saline solution intravenously.
15	4.12½	39 mm.	
16	4.14	43 mm.	
17	4.14½	44 mm.	Stopped injecting saline solution. 250 c.c. were given in 4½ minutes.
18	4.16	42 mm.	
19	4.17	40 mm.	
20	4.31	50 mm.	Began to transfuse.
21	4.32	70 mm.	
22	4.35	85 mm.	
23	4.35½	85 mm.	
24	4.36	93 mm.	Stopped transfusing. Duration, 5 minutes.
25	4.38	100 mm.	
26	4.45	98 mm.	
27	4.55	94 mm.	
28	5.00	96 mm.	The dogs were killed.

Summary.—The blood-pressure of the recipient was reduced 92 mm. by shock. On injecting 250 c.c. of normal saline solution intravenously the pressure was raised but little, and immediately began to fall. On transfusing for five minutes the pressure was raised a

maximum of 60 mm., and maintained within 6 mm. of this level as long as the experiment lasted.

EXPERIMENT 13

Shock; Intravenous Saline Infusion; Transfusion

NOVEMBER 17, 1906.

Donor.—Brown mongrel bitch; weight, 7.2 kilos; condition, good. *Recipient.*—Young black mongrel bitch; weight, 4 kilos; condition, good. Ether anesthesia for both dogs through tracheal cannulæ. The carotid artery of the donor was anastomosed to the femoral vein of the recipient by Carrel's method. The blood-pressure of the recipient was recorded on the drum. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-pressure	Remarks
1	9.55	158 mm.	Began to produce shock in the usual way.
2	10.04	150 mm.	
3	10.15	130 mm.	
4	10.32	118 mm.	
5	10.39	96 mm.	
6	10.45	82 mm.	
7	11.30	64 mm.	
8	12.15	54 mm.	
9	12.27	40 mm.	
10	12.47½	35 mm.	The respiration was poor.
11	12.50	38 mm.	
12	12.51	30 mm.	The heart was weak.
13	12.53	30 mm.	Began to inject normal saline solution intravenously.
14	12.54	36 mm.	$\frac{1}{100}$ grain (0.65 mgm.) strychnin was injected intravenously.
15	12.59	48 mm.	Stopped injecting saline solution. 250 c.c. were given in six minutes.
16	1.06	66 mm.	
17	1.14	76 mm.	Began to inject saline solution again slowly, and gave 200 c.c. in the next nineteen minutes. The total amount injected was 450 c.c.
18	1.25	86 mm.	
19	1.36	80 mm.	
20	1.47	90 mm.	The heart showed evidence of being acutely dilated.
21	2.05	66 mm.	
22	2.24	62 mm.	
23	2.40	60 mm.	
24	2.46	52 mm.	
25	2.47	46 mm.	
26	2.48	44 mm.	
27	2.55	40 mm.	
28	3.10	36 mm.	

Control	Time	Blood-pressure	Remarks
29	3.12	35 mm.	
30	3.15	35 mm.	Began to transfuse.
31	3.18	83 mm.	
32	3.20	90 mm.	
33	3.22	98 mm.	
34	3.25	106 mm.	
35	3.26	104 mm.	
36	3.27	90 mm.	
	3.27½		Stopped transfusion. Duration twelve and a half minutes.
37	3.30	96 mm.	
38	3.35	80 mm.	
39	3.45	64 mm.	
40	4.00	72 mm.	
41	4.10	71 mm.	
42	4.30	71 mm.	The dogs were killed.

Summary.—The blood-pressure of the recipient was reduced 128 mm. by shock. On injecting 450 c.c. of normal saline solution intravenously the pressure rose a maximum of 60 mm. above the low level caused by the shock, and soon fell to within 5 mm. of this level again. Then, on transfusing blood for twelve and a half minutes, the pressure was raised again a maximum of 71 mm., and while the pressure began slowly to fall, it was much better sustained than by the saline solution, and when the experiment ended had not reached as low as the maximum level after the saline solution was given.

Miscellaneous Shock Experiments

EXPERIMENT 14

Transfusion; Attempted Production of Shock; Destruction of the Medulla; Maintenance of Greatly Increased Blood-pressure

May 28, 1907.

Donor.—Dog; weight, 10 kilos; condition, good. *Recipient.*—Dog; weight, 10 kilos; condition, good. Both dogs were anesthetized with ether. The recipient was connected to the manometer and smoked drum via a carotid artery. The left external jugular vein of the recipient was connected to the right common carotid artery of the donor by means of an anastomosis cannula. All data refer to the recipient, unless otherwise specified.

12.09.—Blood-pressure, 174 mm.

12.20.—Began to transfuse for a few seconds at a time at short intervals.

12.30.—Control. Blood-pressure, 190 mm.

12.36.—Control. Blood-pressure, 226 mm. After burning both hind paws and a front paw the pressure rose to 242 mm.

12.45.—Control. Blood-pressure, 180 mm. $\frac{1}{50}$ grain (1.3 mgm.) atropin was injected into the left femoral vein in order to prevent reflex cardiac inhibition.

12.46½.—The medulla was completely destroyed.

12.48.—Control. Blood-pressure, 290 mm. Artificial respiration was begun through a tracheal cannula.

1.18.—Dog killed. The animal was subjected to visceral traumatism for thirty minutes, which was followed by slight change in the blood-pressure.

Autopsy.—The medulla was completely destroyed, and there was also slight destruction of the cerebellum. The lungs and heart were negative. All the blood-vessels were engorged with blood. The abdominal vessels and organs were distended, and there was a small amount of clear fluid in the peritoneal cavity.

Summary.—Following direct transfusion there was a rise in the blood-pressure, which was fairly well sustained. The destruction of the medulla caused no change in the pressure. Severe traumatism without hemorrhage caused no change in the pressure. The animal could not, so far as the circulatory evidence went, be reduced to surgical shock.

EXPERIMENT 15

Transfusion; Destruction of the Medulla; Maintenance of Greatly Increased Blood-pressure

MAY 31, 1907.

Donor.—Dog; weight, 20 kilos; condition, good. *Recipient.*—Dog; weight, 7 kilos; condition, good. Both dogs were anesthetized with ether. Other arrangements were as in the preceding experiment. All data refer to the recipient, unless otherwise specified.

4.30.—Control on drum. Blood-pressure, 160 mm.

4.38.—Transfused slowly for ten minutes.

4.48.—Control. Blood-pressure, 192 mm. The medulla was exposed. A tracheal cannula was inserted into the trachea. Blood-pressure, 180 mm. The medulla was then destroyed and artificial respiration was begun. The blood-pressure rose to 270 mm. The thorax was opened, and the heart exposed and massaged, with a temporary fall in the blood-pressure.

Autopsy.—The medulla was completely severed. The blood-ves-

sels were engorged, and also the organs of the abdominal cavity. The heart and lungs were in fair condition.

Summary.—Transfusion was followed by a marked rise in the blood-pressure, which was sustained. In destroying the medulla the blood-pressure rose markedly. Rough manipulation of the lungs and heart caused relatively small rise in the blood-pressure. The circulation remained more even than in similar manipulation without transfusion.

EXPERIMENT 16

Excessive Transfusion

MAY 27, 1907.

Donor.—Dog; weight, 8 kilos; condition, good. *Recipient.*—Dog; weight, about 7 kilos; condition, good. Both dogs were anesthetized with ether. Other arrangements were as in the preceding experiment. All data refer to the recipient, unless otherwise specified.

4.18.—Control on drum. Blood-pressure, 120 mm. The transfusion was begun and continued intermittently, with the object of allowing as much blood as possible to pass over without causing acute dilatation of the heart.

4.23.—Control. Blood-pressure, 160 mm.

4.26.—Control. Blood-pressure, 150 mm. Edema of the lungs rapidly developed, with a frothy discharge issuing from the mouth and nose. The discharge became serous, then blood-tinged, and finally almost pure blood poured out.

4.37.—Control. Blood-pressure, 80 mm. The dog began to become asphyxiated.

4.38.—Control. Blood-pressure, 122 mm.

4.40.—Control. Blood-pressure, 32 mm. Death occurred.

Autopsy.—There was a very marked engorgement of the right auricle and ventricle of the heart, and an extreme degree of dilatation of all the blood-vessels. Bloody fluid was found in both pleural cavities. Both lungs were almost consolidated. Along the anterior borders there was a slight amount of frothy fluid. On section, exudates of pure blood were found almost everywhere. Pieces removed from the posterior borders sank in water, while pieces from the anterior borders floated. In the abdominal cavity there was a slight amount of clear fluid. The liver was intensely engorged and enlarged.

Summary.—The animal was killed by the production of acute edema of the lungs. The blood flowed under an unusually high pressure. (See Fig. 27.)

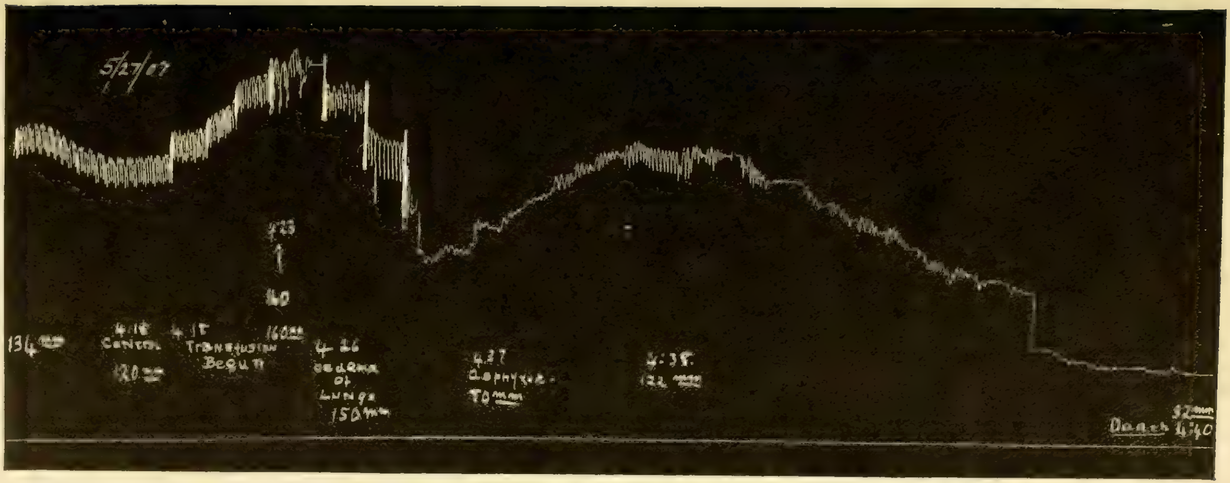


FIG. 27.—EXCESSIVE TRANSFUSION. Death from acute cardiac dilatation and pulmonary edema. (Experiment 16.)

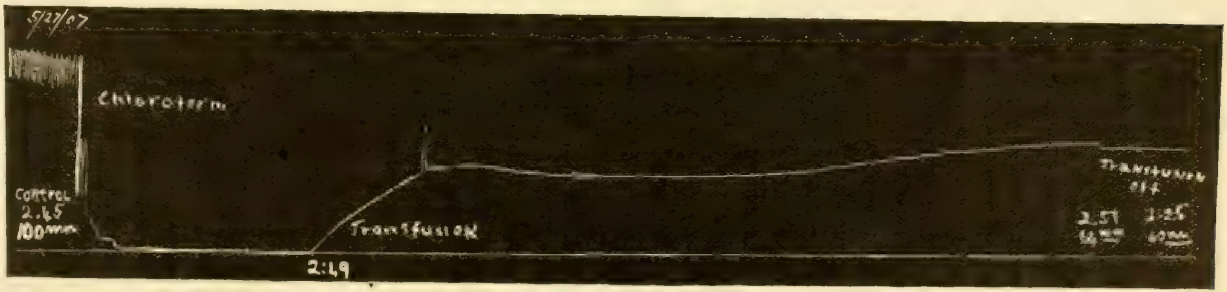


FIG. 28.—AFTER KILLING A DOG WITH CHLOROFORM WITH FALL OF THE BLOOD-PRESSURE TO ZERO, TRANSFUSION RAISED THE BLOOD-PRESSURE (TAKEN FROM A CAROTID ARTERY) TO 64 MM. HG. This shows that the blood-pressure may be raised in a purely mechanical way by means of transfusion. (Experiment 17.)

EXPERIMENT 17

Intentional Chloroform Death; Transfusion

MAY 27, 1907.

Donor.—Dog; weight, 11 kilos; condition, good. *Recipient.*—Black mongrel dog; weight, 6 kilos; condition, good. Both dogs were anesthetized with ether. Other arrangements were as in the preceding experiments. All data refer to the recipient, unless otherwise specified.

2.45.—Control on drum. Blood-pressure, 100 mm.

2.46.—Chloroform was administered until the blood-pressure fell to zero, and death occurred.

2.49.—The transfusion was begun and continued for two minutes. Small waves occurring in the blood-pressure record could not be accounted for unless through accidental interference with the apparatus. The pressure steadily rose.

2.51.—Blood-pressure, 64 mm. The transfusion was stopped, and the vein of the recipient ligatured.

3.05.—Control. Blood-pressure, 64 mm.

Autopsy.—There was no free abdominal fluid. The bladder was full. The vessels were everywhere dilated with venous blood. The liver was enormously distended and of firm consistency. The lungs were clear and there was no free fluid in the pleural cavities. The right heart was engorged with blood.

Summary.—Ordinarily when the blood-pressure is raised to about 60 mm., the normal coronary pressure, the heart resumes its action. In this instance of death from chloroform no contractions of the heart were noted. (See Fig. 28.)

EXPERIMENT 18

Accidental Death; Recovery; Transfusion; Intentional Chloroform Death; Continued Transfusion; Normal Saline Infusion

MAY 28, 1907.

Donor.—Dog; weight, 15 kilos; condition, good. *Recipient.*—Male puppy; weight, 4 kilos; condition, good. Both dogs were anesthetized with ether.

While exposing the vessels in the neck of the recipient "death" occurred—there was complete absence of respiration and cardiac action. The carotid artery was quickly exposed, a cannula inserted, and an infusion of normal saline solution with 2 c.c., 1–1,000, adrena-

lin chlorid solution begun. Artificial respiration was begun. Recovery soon followed. The external jugular vein of the recipient was anastomosed to the common carotid artery of the donor with an anastomosis cannula. Further data refer to the recipient, unless otherwise specified.

3.50.—(After the resuscitation.) Blood-pressure, 82 mm. Transfusion was begun, and carried on intermittently for eight minutes.

3.58.—Transfusion was stopped. Control. Blood-pressure, 110 mm. The recipient was given chloroform.

4.15.—Death occurred. Control. Blood-pressure, 30 mm. The transfusion was begun again, and continued until the pressure reached 72 mm.

4.18.—Control. Blood-pressure, 72 mm.

4.29.—Removed 400 c.c. of blood. Control. Blood-pressure, 12 mm. Transfused again.

4.36.—Control. Blood-pressure, 28 mm. By this time the donor was completely exsanguinated. 500 c.c. of normal saline solution were infused into the external jugular vein of the recipient, and edema of the lungs was produced. The experiment was then stopped.

Autopsy.—The tissues were generally edematous. There was free, slightly hemorrhagic fluid in the peritoneal cavity. The retroperitoneal tissues were dripping with clear, watery fluid. The liver was engorged with blood. The pleural cavities contained slightly hemorrhagic fluid. The lungs were engorged with frothy, bloody fluid. The blood-vessels were everywhere dilated. The right heart was tremendously dilated with blood.

Summary.—This experiment showed that after suspended animation the blood-pressure could be raised 72 mm. by transfusion, but the heart could not be made to beat.

EXPERIMENT 19

Infusion of One Thousand Cubic Centimeters of Normal Saline Solution

MAY 29, 1907.

Dog; weight, 8 kilos; condition, good. Ether anesthesia. A cannula was inserted into the left external jugular vein, and attached by means of a rubber tube to an infusion bottle containing warm normal saline solution. The bottle was placed eight feet above the level of the operating table. The carotid artery was connected with the manometer and smoked drum.

2.21.—Control on drum. Blood-pressure, 134 mm.

2.24.—The infusion was slowly begun. Blood-pressure, 140 mm.

2.26.—Control. Blood-pressure, 116 mm.

2.29.—Control. Blood-pressure, 140 mm. 800 c.c. were infused.

2.42½.—1,000 c.c. were infused. Blood-pressure, 98 mm. Edema of the lungs occurred.

Autopsy.—There was a large amount of clear fluid in the peritoneal cavity, and the retroperitoneal tissues were dripping clear fluid. There was also a large amount of clear fluid in the peritoneal sac and in both pleural cavities. There was edema of both lungs and of the tissues of the neck.

Summary.—This experiment was made to contrast the negative effect of overinfusion of normal salt solution as compared with overtransfusion of blood. An equal amount of blood would have caused a marked rise in the blood-pressure.

EXPERIMENT 20

Excessive Transfusion

May 29, 1907.

Donor.—Dog; weight, 18 kilos; condition, good. *Recipient.*—Dog; weight, 8 kilos; condition, good. Both dogs were anesthetized with ether. The left external jugular vein of the recipient was sutured to the left common carotid artery of the donor. Other arrangements were as in the previous experiments. All data refer to the recipient, unless otherwise specified.

3.40.—Control on drum. Blood-pressure, 150 mm. The transfusion was begun, and was allowed to go on slowly for eighteen minutes, when the blood-pressure was 186 mm.

4.18.—Transfused again slowly for twenty-three minutes.

4.41.—Edema of the lungs developed. Control. Blood-pressure, 186 mm.

4.48.—Control. Blood-pressure, 110 mm. 90 c.c. of fluid were lost by mouth.

4.55.—Death occurred. Control. Blood-pressure, 26 mm.

Autopsy.—Clear fluid was found in the abdomen and pericardial sac. All the abdominal viscera were engorged. Bloody fluid was found in both pleural cavities, and there was marked edema and hemorrhage of both lungs. The right auricle and ventricle were engorged with blood.

Summary.—When edema of the lungs once appears it is impossible to raise the blood-pressure, or to sustain it by overtransfusion. This is partly because of the large loss of fluid by mouth, and partly

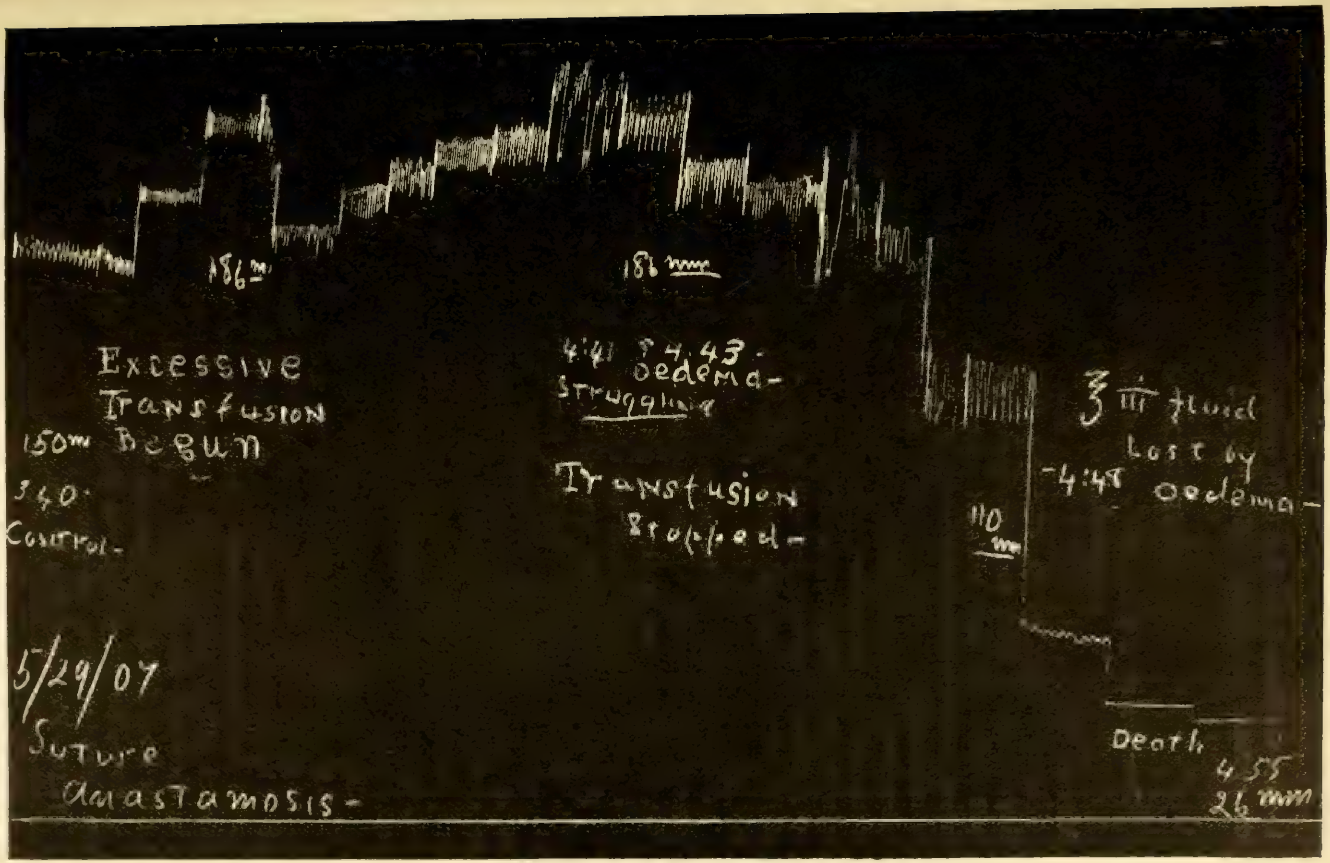


FIG. 29.—EXCESSIVE TRANSFUSION. Death from acute cardiac dilatation and pulmonary edema. (Experiment 20.)

because the blood is blocked in its transference from the pulmonic to the systemic circulation. (See Fig. 29.)

EXPERIMENT 21

Transfusion; Section of the Spinal Cord below the Medulla; Decapitation; Autopsy

May 11, 1907.

Donor.—Dog; weight, 18 kilos; condition, good. *Recipient.*—Dog; weight, 4 kilos; condition, good. Both dogs were anesthetized with ether. The recipient's left external jugular vein was anastomosed to the right common carotid artery of the donor by means of an anastomosis tube, the cervical spinal cord was carefully dissected out near the medulla, and the carotid artery was connected to the manometer and the smoked drum in the usual way. All further data refer to the recipient, unless otherwise specified.

11.26.—Control on drum. Blood-pressure, 83 mm. The resection of the vertebræ and the attending hemorrhage accounted for the low pressure.

11.27.—Control. Blood-pressure, 83 mm. Transfused for ten seconds. The pressure rapidly rose to 128 mm., and fell at once to 86 mm. It then rose to 120 mm., and finally fell again.

11.40.—Control. Blood-pressure, 106 mm.

11.50½.—Transfused for one minute. The pressure rose to 118 mm., and fell a little, and ultimately rose to 130 mm.

11.53.—Destroyed the medulla. At the same time transfusion was begun again. Artificial respiration was started. The cord was then resected below the medulla. The pressure immediately fell to 74 mm. after destroying the medulla, but after beginning the transfusion it rose, and averaged 90 mm. The transfusion was maintained for two minutes.

11.55.—Control. Blood-pressure, 140 mm.

11.58.—Control. Blood-pressure, 140 mm.

11.59.—Control. Blood-pressure, 132 mm. From 11.55 the length of the heart stroke as recorded on the drum was shortened, owing to partial clotting in the carotid cannula. The clot was removed. Amputation of the head was begun. Transfusion was begun, and was continued until the amputation was completed, in order to make up for the blood lost during the operation.

12.01.—The amputation was completed. Considerable blood was lost. Blood-pressure, 100 mm.

12.10.—Blood-pressure, 86 mm.

12.14.—Blood-pressure, 90 mm., and showed no sign of falling.

12.17.—With the heart still beating, and artificial respiration still being performed, the autopsy was begun. The liver was normal in appearance. The splanchnic arteries were filled with blood, and were pulsating. The arterial blood could be changed to venous blood at will by simply stopping the artificial respiration, and on continuing it this was reversed. The bladder was full. The diaphragm showed a slight convulsive action of its muscles on stopping the artificial respiration.

12.20.—The action of the heart caused pulsations in the air in the tracheal tube.

12.24½.—The blood in the skin was of normal appearance.

12.29.—With the chest widely opened the heart still beat regularly. As soon as artificial respiration was stopped the veins became engorged with blood.

12.29½.—The respiration was started, and the arteries showed arterial blood.

12.29¾.—The respiration was stopped, and the arteries showed venous blood.

12.30.—The respiration was started, and the arteries showed arterial blood.

12.30½.—The respiration was stopped, and the arteries showed venous blood.

12.30¾.—The respiration was started, and the arteries showed arterial blood.

12.31.—The respiration was stopped, and the arteries showed venous blood. After all this lapse of time and all these different procedures the heart still beat strongly and regularly. The dog was finally " killed " by stopping the artificial respiration.

Summary.—This experiment demonstrates that the circulation of decapitated overtransfused animals may continue for a certain period of time if artificial respiration is maintained. (See Figs. 30, *a–d.*)

EXPERIMENT 22

Transfusion; Attempted Production of Shock; Destruction of the Medulla

MAY 16, 1907.

Donor.—Mongrel dog; weight, about 18 kilos; condition, good. Recipient.—Black mongrel bitch; weight, 5 kilos; condition, good. Both dogs were anesthetized with ether. All further data refer to the recipient, unless otherwise specified.

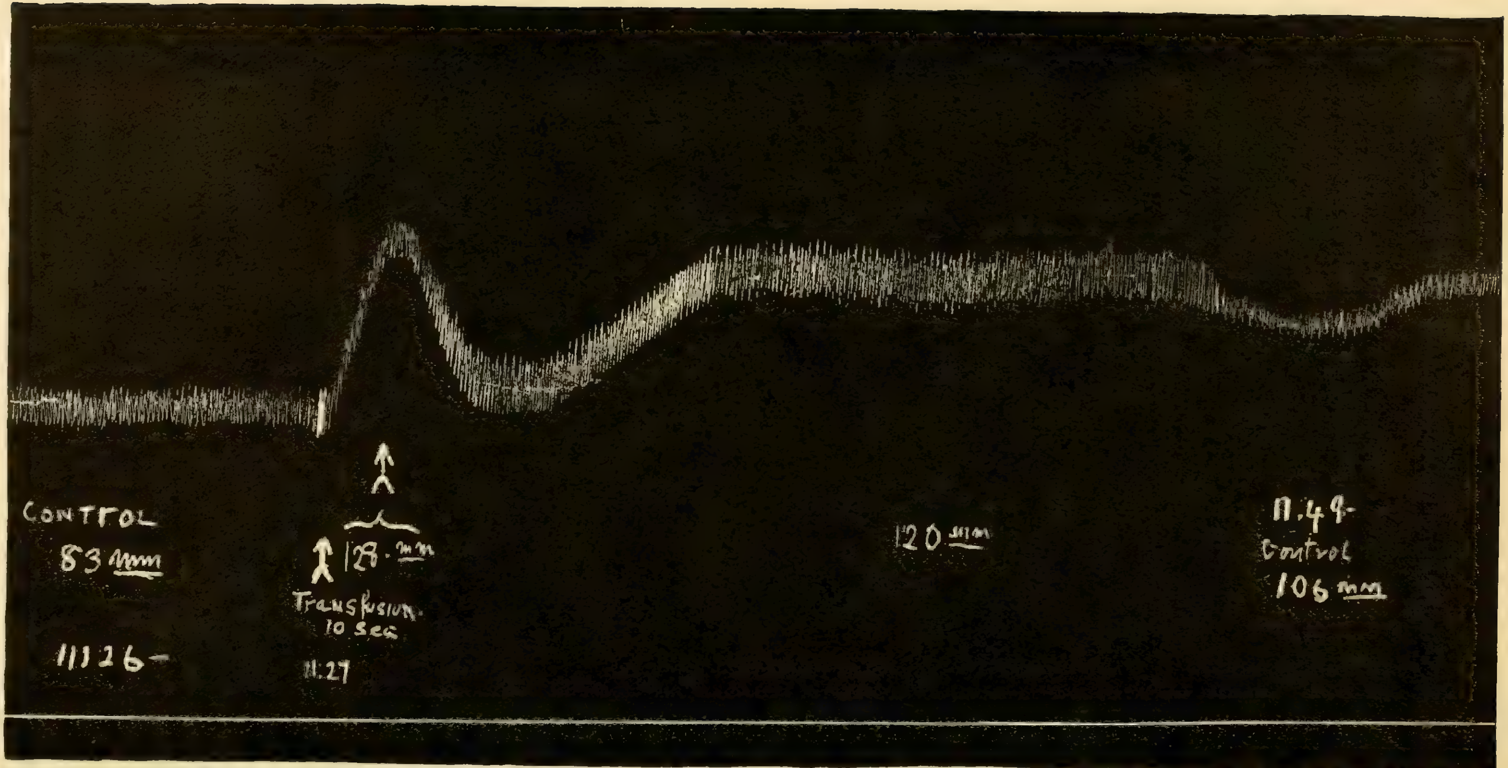


Fig. 30 *a*.—Transfusion, Destruction of the Medulla and Section of the Spinal Cord Below the Medulla, Maintenance of Artificial Respiration, Amputation of Head, Continuance of Circulatory Activity until the Termination of the Experiment. Note that the blood-pressure was slightly higher at the end of the experiment than at the beginning. (Experiment 21.) (See also continuation, Figs. 30 *b*, *c*, *d*.)

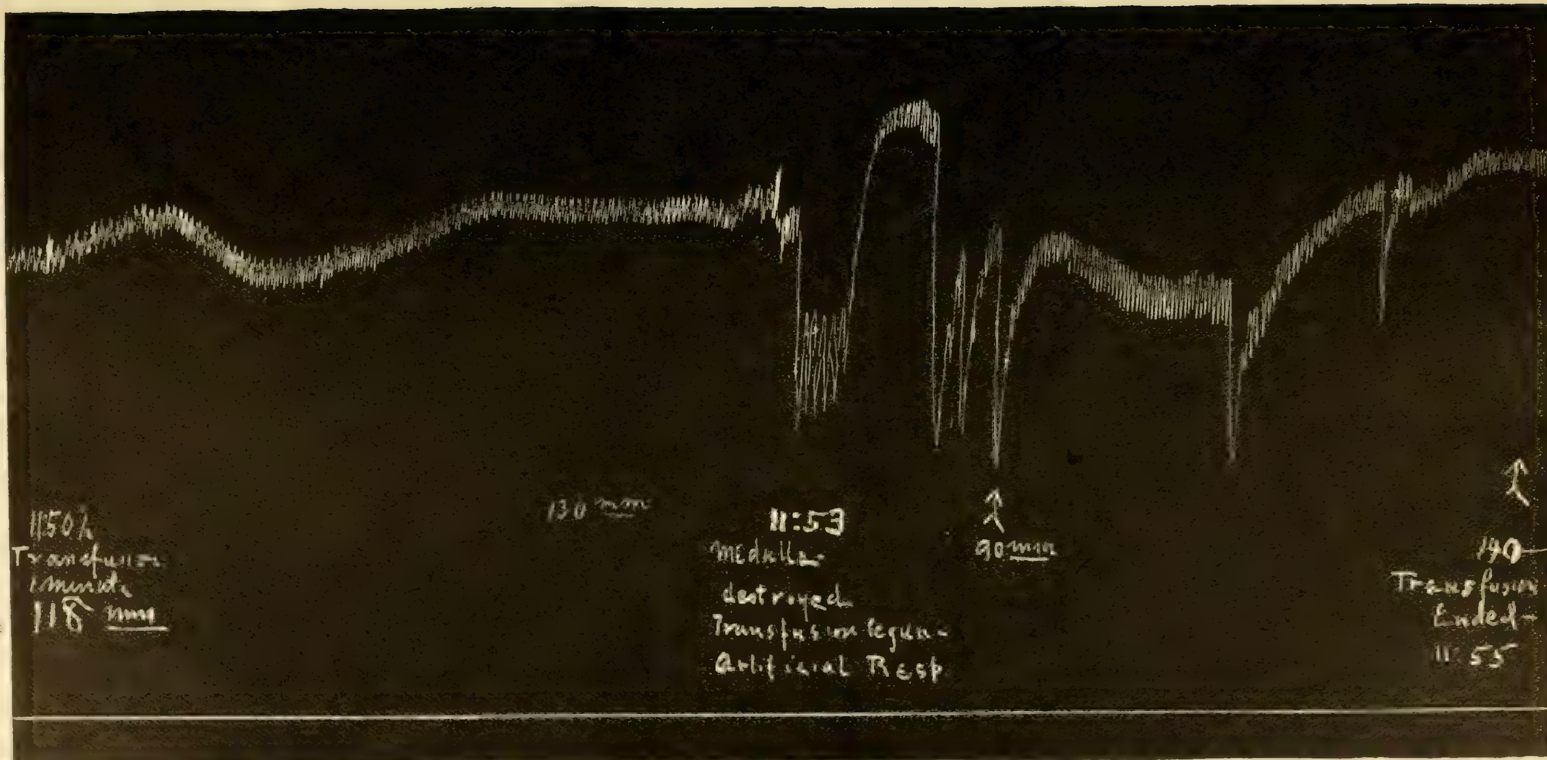


Fig. 30 *b*.—Continuation of Fig. 30 *a*.

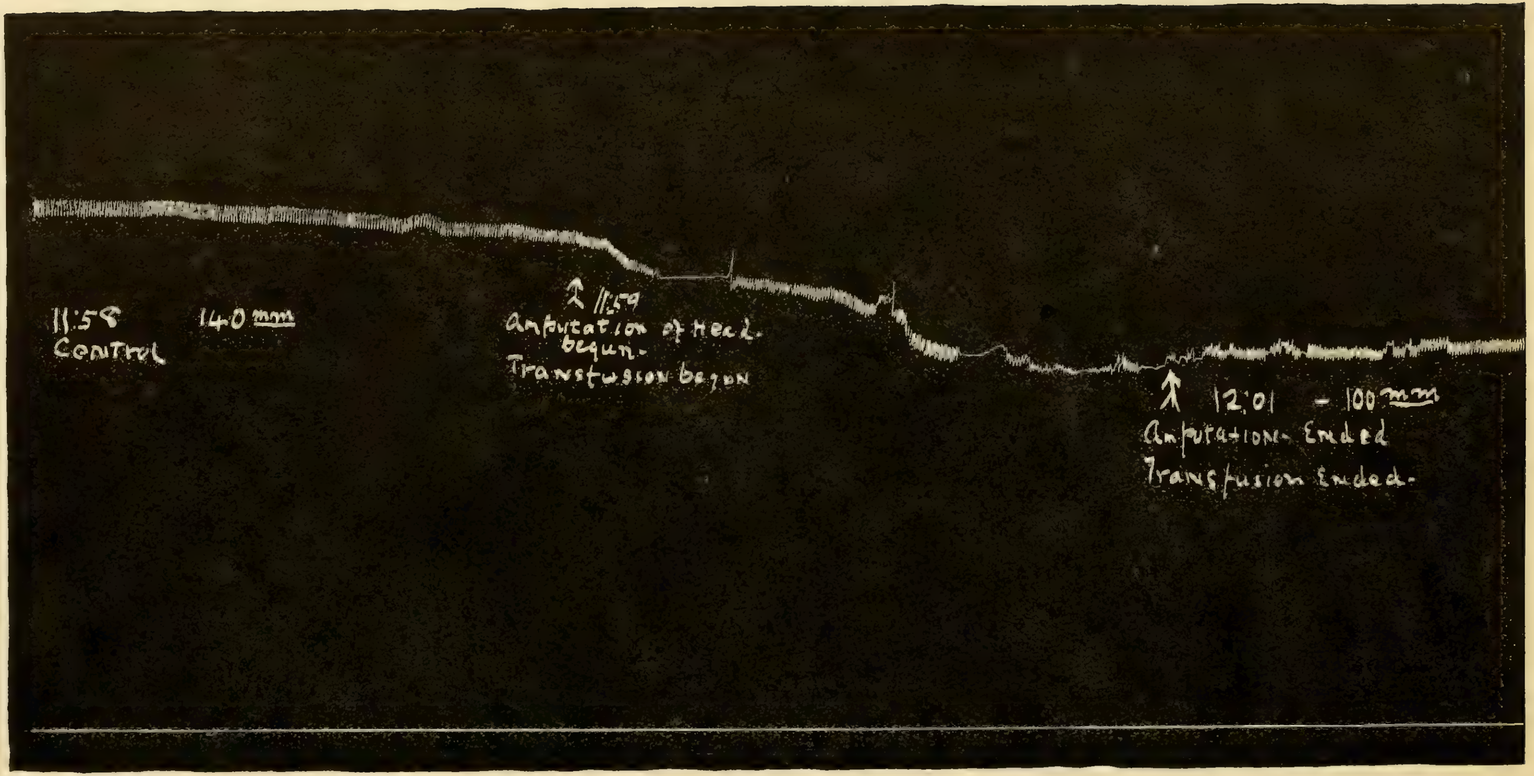


FIG. 30 *c*.—Continuation of Fig. 30 *b*.

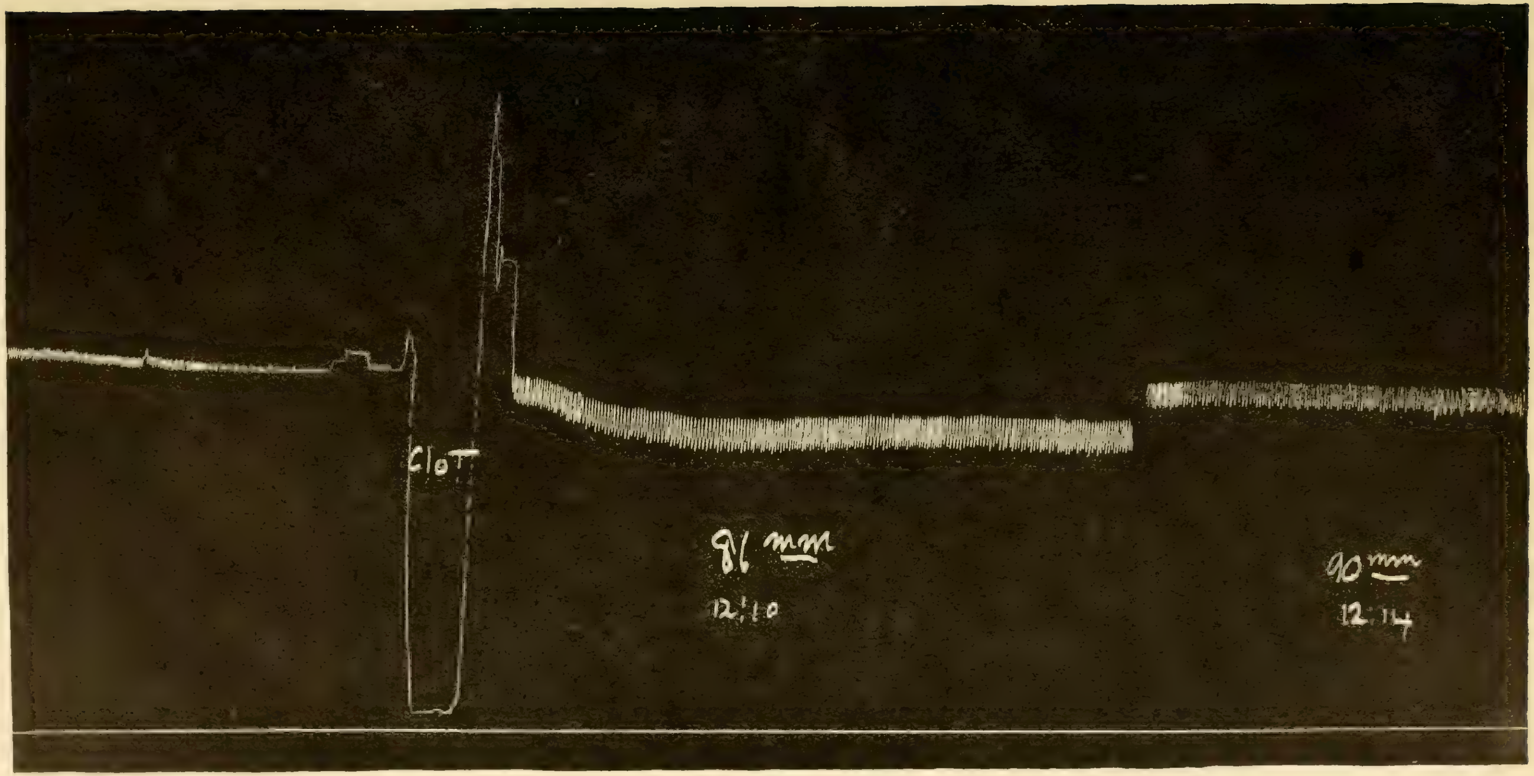


FIG. 30 *d*.—Continuation of Fig. 30 *c*.

3.58½.—The left carotid artery of the donor was anastomosed by means of a large anastomosis cannula to the right external jugular vein of the recipient. The right carotid artery of the recipient was connected with the manometer and smoked drum.

4.23½.—Control. Blood-pressure, 190 mm. Up to this time the recipient had been under ether for twenty-five minutes.

4.28½.—Control. Blood-pressure, 168 mm.

4.33½.—Control. Blood-pressure, 146 mm.

4.38½.—Control. Blood-pressure, 146 mm.

4.43½.—Control. Blood-pressure, 146 mm. The transfusion was started, and continued for four and a half minutes.

4.45½.—Control. Blood-pressure, 182 mm.

4.46½.—Control. Blood-pressure, 192 mm.

4.47.—Control. Blood-pressure, 200 mm.

4.48.—The transfusion was stopped.

4.49.—Control. Blood-pressure, 214 mm. The transfusion was started again.

4.50.—Control. Blood-pressure, 230 mm. The transfusion was stopped. The flow was excellent.

4.51½.—Control. Blood-pressure, 200 mm. The abdomen was opened by a long incision. All the vessels which were severed bled profusely. The vessels of the mesenteries and the intestines were engorged with blood. There was no free blood in the peritoneal cavity. The liver was markedly enlarged, firm, and of rubberlike consistency. The spleen was distended, and of firmer consistency than normal. The intestines were allowed to come out of the peritoneal cavity, and were exposed to the air, and the parietal and visceral peritoneum was vigorously manipulated almost constantly during the remainder of the experiment in order to try to produce shock. The dilatation of the splanchnic vessels was so marked that the rubbing caused blood to ooze out almost everywhere. The liver was also manipulated, and oozed in the same way.

4.55.—Control. Blood-pressure, 176 mm.

5.00.—Control. Blood-pressure, 168 mm. In a further effort to produce shock the right hind paw was deeply burned. The only effect was an increase in the respiratory rate.

5.01.—Control. Blood-pressure, 168 mm. The left hind paw was burned, with the same result.

5.02½.—Control. Blood-pressure, 180 mm.

5.03.—Control. Blood-pressure, 180 mm. The right sciatic nerve was exposed, with some hemorrhage occurring during the operation. Peripheral and central traction was exerted, and torsion, and the

nerve was rubbed so much that it finally was rubbed through. The only effect was to increase the respiratory rate.

5.12.—Control. Blood-pressure, 160 mm. The right fore paw was burned, with slight increase in the respirations following. The blood-pressure remained the same.

5.13.—On compressing the thorax there was a slight rise in the blood-pressure.

5.21.—Transfused for two seconds. This was to replace partially the blood lost through the constant oozing from the liver and peritoneal surfaces. Blood-pressure, 172 mm.

5.22.—Transfused for two seconds.

5.24.—Inserted a tracheal tube. Exposed the cervical cord. There was considerable hemorrhage from the skin and fascia, and there was constant oozing from the posterior cervical vessels.

5.29½.—Transfused for twenty seconds.

5.31.—The medulla was destroyed by passing forceps up through the spinal canal. Respiration ceased at once, and the blood-pressure began to fall at once, the mean lowest pressure being 122 mm.

5.31½.—Artificial respiration was begun, and the blood-pressure immediately rose to 132 mm. at first, and then rose gradually to 180 mm., *without further transfusion.*

5.34.—Transfused for fifteen seconds to compensate for the oozing.

5.35.—Transfused for fifteen seconds.

5.36½.—Transfused for one minute. Control. Blood-pressure, 160 mm. Up to this time the attempts to produce shock had lasted forty-four minutes, and during the forty-four minutes the blood-pressure had fallen only 40 mm.

5.40½.—The artificial respiration was stopped. Control. Blood-pressure, 158 mm.

5.41.—Control. Blood-pressure, 126 mm.

5.43.—Control. Blood-pressure, 94 mm.

5.45.—Control. Blood-pressure, 56 mm.

5.45½.—Control. Blood-pressure, 40 mm.

5.47.—Control. Blood-pressure, 22 mm. The heart stopped beating.

5.52.—Control. Blood-pressure, 16 mm. There was no further fall in the blood-pressure.

6.03.—*Autopsy.*—The pupils were dilated. The conjunctivæ were clear. The nose was clean, and showed no sign of hemorrhage. There was no bloody mucus in the mouth. The veins under the tongue were congested. Black fluid blood dripped from

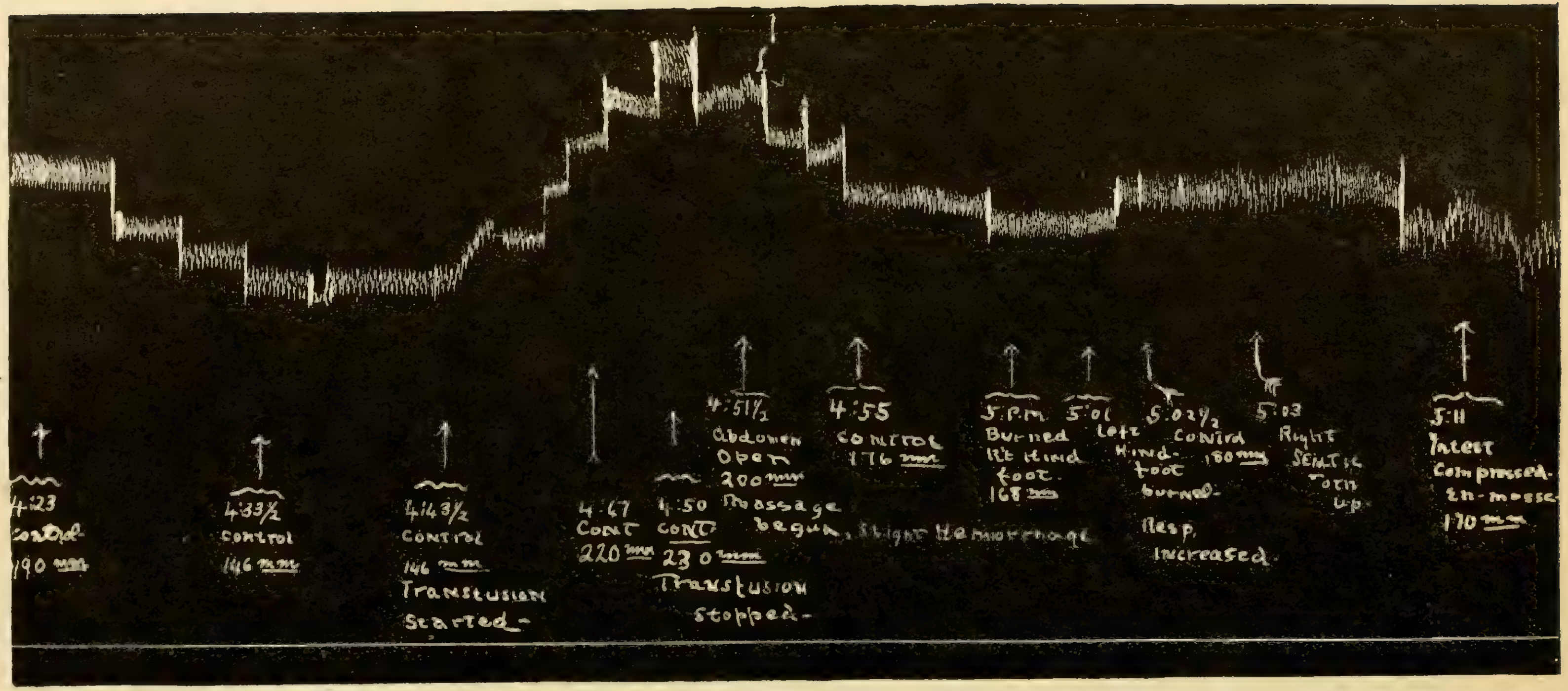


FIG. 31 *a*.—UNSUCCESSFUL ATTEMPT TO PRODUCE SHOCK AFTER TRANSFUSION. Destruction of the medulla without lowering of the blood-pressure or cessation of circulation until artificial respiration was stopped. (Experiment 22.)

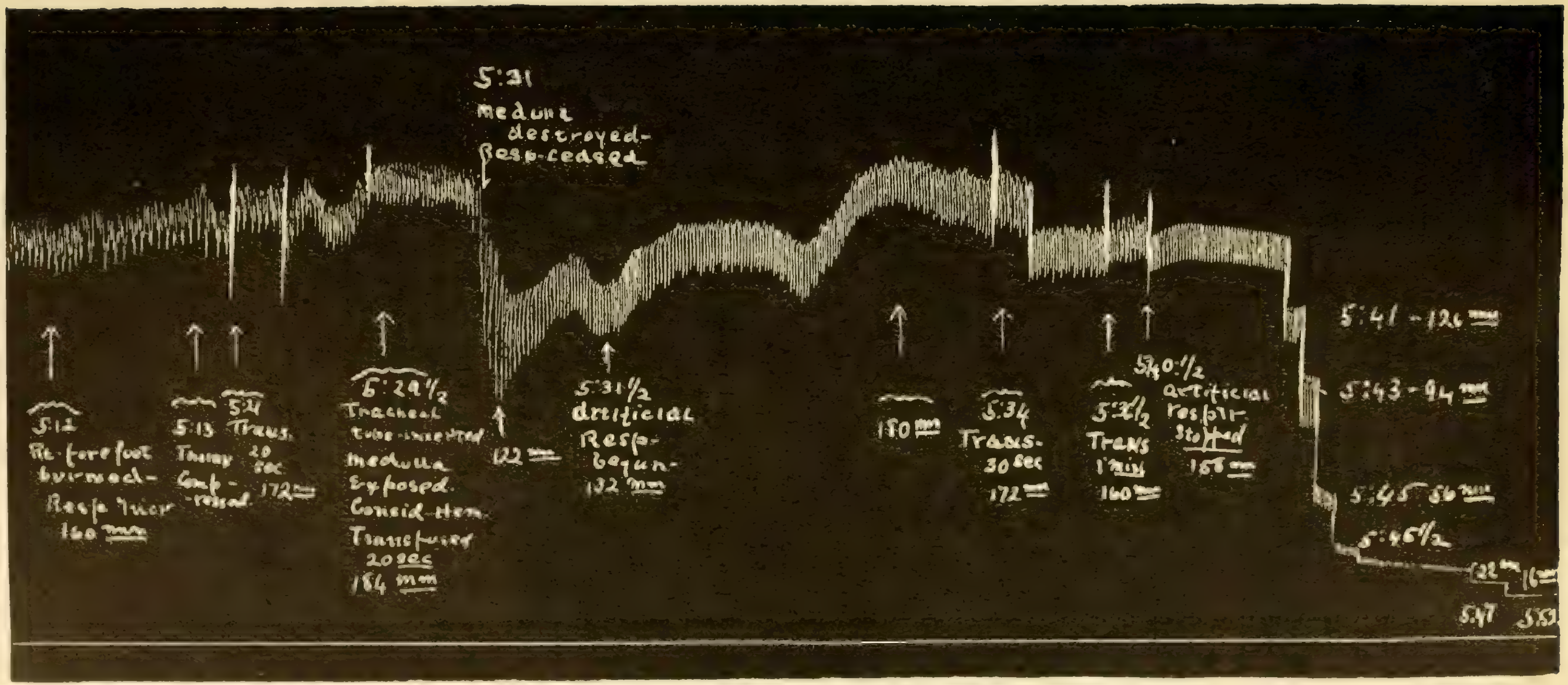


Fig. 31 *b*.—Continuation of Fig. 31 *a*.

the carotid cannula. There was no bleeding from the freshly severed external jugular vein. There was no bloody mucus in the tracheal cannula.

Thorax.—The veins on the under surface of the sternum were congested. In the pleural cavities there was free fluid blood. The lungs were of fairly good color, and contained no hemorrhages or consolidations. The trachea was clear. The pericardium was normal, and contained about 4 c.c. of clear, straw-colored fluid. The right heart was dilated with very dark fluid blood. There were no clots. The auricle and ventricle and the valves were normal. The left heart was normal. The aorta was normal. The coronary arteries were patent. The coronary veins were filled with dark blood.

Abdomen.—The parietal and visceral peritoneum was injected and hemorrhagic. There were about 60 c.c. of clotted blood in the peritoneal cavity. The liver was enlarged and distended, of firm consistency, dark color, and covered with bleeding points. There were many small clots, and the surface was broken in many places. The lobules were distinctly outlined. On section the cut surfaces dripped freely. The gall bladder was distended with bile. The spleen was distended and firm, and on section the cut surfaces dripped freely. The pancreas seemed to be normal. The capsular veins of the right kidney were injected. On section the surfaces seemed to be normal, and dripped blood. The same was true of the left kidney. The ureters were normal. The bladder was not distended. The uterus was normal. The vessels on the surface of the stomach were normal. There was no blood inside of the stomach. The mucous membrane was normal. In the small intestine there was a hemorrhage in the wall 7 cm. from the pylorus, and another 21 cm. from the pylorus. Three intestinal worms were found. The appendix was normal. The vessels of the cerebral dura mater were engorged, and there were hemorrhages at the base of the brain. The cerebellum was lacerated. The medulla was torn to shreds in the lower portion, and markedly torn and lacerated in the upper portion. The cervical cord was macerated, and there was a hemorrhage in the cord.

Summary.—In this experiment it was impossible to produce fatal shock immediately by destruction of the medulla, owing to the blood-pressure being maintained by the transfusion. Despite the shock resulting from the procedures, the alterations of the pressure depended entirely on the other factors. (See Figs. 31, *a* and *b*.)

Comparison of Transfusion and Saline Infusion in the Treatment of Combined Hemorrhage and Shock

EXPERIMENT 23

Combined Hemorrhage and Shock; Intravenous Saline Infusion; Transfusion

October 16, 1906.

Donor.—Mongrel bull bitch; weight, 10.8 kilos; condition, good. *Recipient.*—Mongrel collie dog; weight, 12.6 kilos; condition, good. Ether anesthesia. The femoral vein of the recipient was fitted with a cannula through which the dog was bled, and through which the saline infusion was injected. The carotid artery of the donor was anastomosed to the other femoral vein of the recipient by Carrel's method. The blood-pressure was recorded in the usual way. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	10.40	135 mm.	
2	11.00	154 mm.	
	11.01		50 c.c. of blood were removed.
3	11.10	140 mm.	
	11.11		50 c.c. of blood were removed.
4	11.23	122 mm.	
	11.25		50 c.c. of blood were removed. Began to produce shock.
5	11.42	117 mm.	
	11.45		50 c.c. of blood were removed. Continued the manipulation.
6	11.46	108 mm.	
	11.47		Continued the manipulation.
7	11.52	72 mm.	
	11.54		50 c.c. of blood were removed. Continued the manipulation.
	12.00		50 c.c. of blood were removed.
	12.10		50 c.c. of blood were removed.
	12.22		50 c.c of blood were removed.
	12.25		50 c.c of blood were removed. Total amount of blood removed, 450 c.c.
8	12.28	58 mm.	
9	12.34	42 mm.	
10	12.38	40 mm.	
11	12.40	53 mm.	Began to inject normal saline solution intravenously.
12	12.46	73 mm.	50 c.c. saline injected.
13	12.48	66 mm.	50 c.c. saline injected.
14	12.50	80 mm.	50 c.c. saline injected.
15	12.51	85 mm.	50 c.c. saline injected.

Control	Time	Blood-Pressure	Remarks
16	12.52	90 mm.	50 c.c. saline injected.
17	12.53	93 mm.	50 c.c. saline injected.
18	12.55	96 mm.	50 c.c. saline injected.
19	12.57	92 mm.	50 c.c. saline injected.
20	1.00	94 mm.	50 c.c. saline injected. Total amount injected, 450 c.c.
21	1.03	90 mm.	
22	1.18	78 mm.	
23	1.30	74 mm.	
24	1.45	75 mm.	
25	2.15	65 mm.	
26	2.45	50 mm.	
27	3.00	41 mm.	
28	3.20	30 mm.	
29	3.40	24 mm.	
30	3.44	20 mm.	Began to transfuse.
31	3.45	86 mm.	
32	3.46	90 mm.	
33	3.47	104 mm.	
	3.52½		Stopped transfusing. Duration, eight and a half minutes.
34	3.54	118 mm.	
35	3.56	128 mm.	
36	3.58	126 mm.	
37	4.10	132 mm.	
38	4.19	130 mm.	
39	4.45	122 mm.	
40	5.00	116 mm.	
41	5.15	110 mm.	
42	5.30	108 mm.	
43	5.45	106 mm.	
44	6.00	104 mm.	Both dogs were killed.

Summary.—The blood-pressure of the recipient was reduced 95 mm. from the original level by the production of shock and the removal of 450 c.c. of blood. On replacing the blood lost by an equal amount of normal saline solution, the blood-pressure at the highest point was brought back but 56 mm., and was not maintained, but fell 20 mm. lower than the first reduction of 95 mm. At the end of a transfusion of blood of eight and a half minutes this lowest level was raised 84 mm. In seventeen and a half minutes more the maximum rise caused by the transfusion was reached—an additional gain of 28 mm., or a total rise of 112 mm. The maximum rise brought the pressure back to within 3 mm. of the original level. Moreover, in one hour and fifty minutes after the maximum level was reached, the pressure fell but 28 mm., so that it was well maintained by the transfusion of blood, in contrast to its not being maintained at all by the saline infusion.

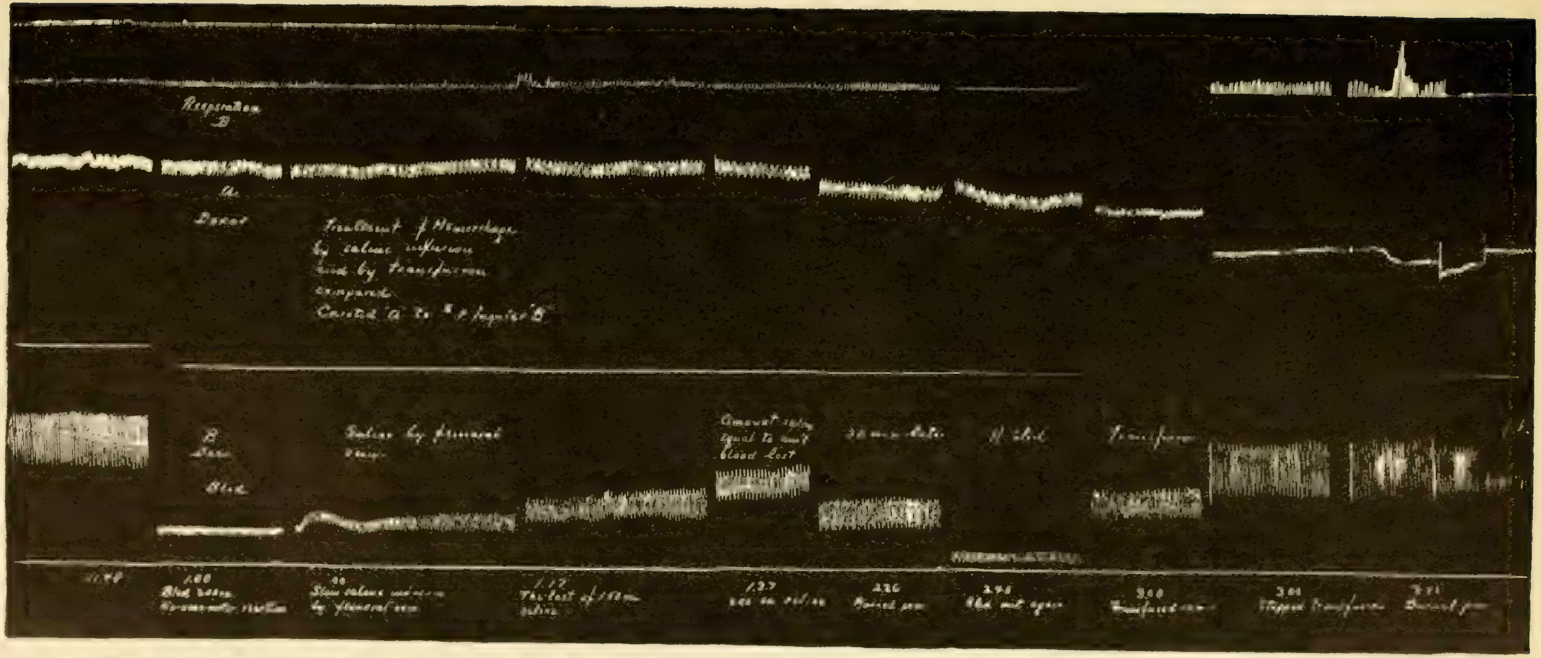


Fig. 32.—The Relative Efficiency of Saline Infusion and Transfusion in the Treatment of Acute Hemorrhage as Shown by the Successive Use of the Two Methods on the Same Dog. The tracings of the donor are shown above and of the recipient ("donee" on record) below. The respirations of the recipient were not recorded, only the blood-pressure.

EXPERIMENT 24

Combined Hemorrhage and Shock; Intravenous Saline Infusion; Transfusion

November 5, 1906.

Donor.—Brown mongrel bitch; weight, 4.5 kilos; condition, good. *Recipient.*—White mongrel bitch; weight, 5.4 kilos; condition, good. Ether anesthesia. A cannula was placed in one of the femoral veins of the recipient, through which the dog was bled, and through which the saline infusion was injected. The carotid artery of the donor was anastomosed to the other femoral vein of the recipient. The blood-pressure was recorded in the usual way. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	10.30	132 mm.	50 c.c. of blood were removed.
2	10.37	84 mm.	50 c.c. of blood were removed.
3	10.45	68 mm.	Began to produce shock.
4	10.55	58 mm.	50 c.c. of blood were removed.
5	10.59	34 mm.	50 c.c. of blood were removed. Produced more shock.
6	11.35	28 mm.	50 c.c. of blood were removed. Total amount of blood removed, 250 c.c.
7	12.05	19 mm.	
8	12.11	21 mm.	Began to inject normal saline solution intravenously.
9	12.15	30 mm.	
10	12.18	36 mm.	
11	12.23	42 mm.	Stopped injecting saline solution. Total amount given, 250 c.c.
12	12.35	30 mm.	
13	12.58	20 mm.	
14	1.01½	16 mm.	
15	1.09	20 mm.	Began the transfusion.
16	1.11	32 mm.	
17	1.14	38 mm.	
18	1.15	42 mm.	
19	1.16	44 mm.	
20	1.24	45 mm.	Stopped the transfusion. Duration, fifteen minutes.
21	1.30	35 mm.	
22	1.45	36 mm.	
23	2.15	30 mm.	Death occurred.

Summary.—The blood-pressure of the recipient was reduced 113 mm. from the original level by the production of shock and the removal of 250 c.c. of blood. On replacing the blood lost by an equal

amount of normal saline solution the pressure was brought back only 23 mm. at the highest point, and almost immediately fell again to a point 3 mm. lower than the original level. After a transfusion of fifteen minutes the pressure was raised again, but only 3 mm. higher than it was raised by the saline (26 mm.). The pressure then began gradually to fall, and death occurred in fifty-one minutes. While the pressure was not well maintained by the transfusion, it was maintained much better than by the saline infusion.

EXPERIMENT 25

Combined Hemorrhage and Shock; Intravenous Saline Infusion; Transfusion

OCTOBER 30, 1906.

Donor.—Tan and white mongrel bitch; weight, 12.6 kilos; condition, good. *Recipient.*—Tan mongrel dog; weight, 4.5 kilos; condition, good. Ether anesthesia. A cannula was placed in one of the femoral veins of the recipient, through which the blood was removed and the saline infusion injected. The carotid artery of the donor was anastomosed to the other femoral vein of the recipient by Carrel's method. The blood-pressure was recorded in the usual way. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	9.55	118 mm.	
2	10.10	102 mm.	50 c.c. of blood were removed.
3	10.13	78 mm.	
	10.25		50 c.c. of blood were removed. Began to produce shock.
4	10.33	52 mm.	
	10.40		Produced more shock.
	11.00		50 c.c. of blood were removed.
5	11.08	34 mm.	
	11.15		Produced more shock.
	11.20		25 c.c. of blood were removed. Total amount removed, 175 c.c.
6	11.22	30 mm.	
	11.25		Began to inject normal saline solution intravenously.
7	11.30	38 mm.	
	11.34		Injected $\frac{1}{250}$ grain strychnin (0.26 mgm.) intravenously.
8	11.35	48 mm.	
9	11.40	54 mm.	Stopped injecting the saline solution. Total amount given, 175 c.c.
10	11.47	64 mm.	

Control	Time	Blood-Pressure	Remarks
11	12.03	51 mm.	
12	12.48	33 mm.	
13	1.07	22 mm.	Transfused for one and a quarter minutes.
14	1.07¾	90 mm.	
15	1.08¼	130 mm.	
16	1.12	135 mm.	
17	1.16	124 mm.	
18	1.20	110 mm.	
19	1.22	96 mm.	
20	1.29	89 mm.	
21	1.44	87 mm.	
22	2.00	84 mm.	
23	2.15	84 mm.	
24	2.30	80 mm.	
25	2.45	54 mm.	
26	3.00	18 mm.	Death occurred.

Summary.—The blood-pressure of the recipient was reduced from the original level 88 mm. by the production of shock and the removal of 175 c.c. of blood. On replacing the blood lost with an equal amount of normal saline solution the blood-pressure was brought back but 34 mm. at the most, and immediately began to fall, although less rapidly than in some of the other experiments, and went 8 mm. lower than the original level. About five minutes after a transfusion of one and a quarter minutes the pressure was raised to a maximum height of 113 mm., or to a point 17 mm. higher than the original level, and from this fell gradually 117 mm. to death in one hour and forty-eight minutes.

EXPERIMENT 26

Combined Hemorrhage and Shock; Intravenous Saline Infusion; Transfusion

October 4, 1906.

Donor.—Mongrel dog; weight, 8.6 kilos; condition, good. *Recipient.*—Mongrel dog; weight, 9.9 kilos; condition, good. Ether anesthesia. A cannula was inserted in one femoral vein of the recipient, through which blood was removed and the saline infusion given. The carotid artery of the donor was anastomosed to the other femoral vein of the recipient. The blood-pressure was recorded on a drum. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	10.45	124 mm.	50 c.c. of blood were removed. Shock was begun, and kept up almost continuously.
2	10.57	104 mm.	
3	11.09	84 mm.	
4	11.15	86 mm.	50 c.c. of blood were removed.
5	11.37	54 mm.	40 c.c. of blood were removed.
6	11.59	30 mm.	60 c.c. of blood were removed. Total amount removed, 200 c.c.
7	12.55	26 mm.	Stopped producing shock.
	12.58½		Began to inject normal saline solution.
	12.59		Injected $\frac{1}{200}$ grain strychnin (0.32 mgm.) intravenously.
8	1.00½	26 mm.	
9	1.02	34 mm.	
10	1.06	38 mm.	
11	1.09	40 mm.	
	1.12		Stopped injecting normal saline solution. Total amount injected, 200 c.c.
12	1.23	51 mm.	
13	2.20¼	24 mm.	
	2.21½		Began to transfuse.
14	2.22	24 mm.	
15	2.24	48 mm.	
16	2.27½	58 mm.	
17	2.29½	62 mm.	
18	2.32	72 mm.	
19	2.40	66 mm.	
	2.40½		Stopped transfusion. Duration, nineteen minutes.
20	2.47½	66 mm.	
21	2.49	60 mm.	
22	3.15	60 mm.	
23	3.35	54 mm.	
24	4.00	56 mm.	
25	4.20	56 mm.	The dog was killed.

Summary.—The blood-pressure of the recipient was reduced 98 mm. from the original level by the production of shock and the removal of 200 c.c. of blood. On replacing the blood lost with an equal amount of normal saline solution the blood-pressure at the highest point was brought back but 25 mm., and immediately fell 2 mm. lower than the first reduction of 98 mm. At the end of a transfusion of nineteen minutes this lowest level was raised but 42 mm., and did not go higher. This maximum point was 58 mm. lower than the original level, but was maintained for one hour and thirty-two and a half minutes, with a fall in this time of but 10 mm. Hence the pressure was much better maintained by transfusion of blood than by saline infusion.

CONCLUSIONS

1. In proper amount and at a proper rate of flow direct transfusion between two dogs may be safely accomplished by the end-to-end anastomosis of an artery of one to a vein of the other. Leakage at the point of junction, as well as obstruction by clotting and the liberation of air or blood clot emboli into the circulation of the recipient, may be avoided by making the anastomosis by either the suture method (Carrel) or the cannula method. The essential part of both methods is that the intima of one vessel comes in contact only with the intima of the other. Many observations apparently indicate that harmful hemolytic action does not occur in dogs—the blood of dogs is physiologically interchangeable.

2. Transfusion is an ideal treatment for acute hemorrhage of any degree of severity in normal dogs. Even after complete cessation of respiration and efficient cardiac action, as long as there is an auricular or feeble ventricular beat, other methods of treatment having failed completely, a dog can usually be resuscitated by direct transfusion.

3. Transfusion is a better form of treatment for shock alone, or combined hemorrhage and shock, than any other known form of treatment. The blood-pressure is raised, it is better sustained than by other fluids, and the rapidly occurring improvement is greater than that obtained by the use of fluids other than blood.

4. The use of infusions of saline solution or other artificial sera is not as efficacious as transfusion of blood in treating shock, combined hemorrhage and shock (or hemorrhage alone), because the former cannot be injected in as great an amount as the amount of blood which may be transfused without passing out of the vascular system of the recipient. Consequently, the blood-pressure is not so

well sustained, and while the improvement is rapid it is less marked.

5. Transfusion, to a certain extent (saline infusion less so), acts independently of the vasomotor centers in raising the blood-pressure—its action is partly mechanical. When the vasomotor centers retain any vitality, transfusion increases it. At the same time the heart is able to act more efficiently by reason of the mechanically raised blood-pressure.

NOTE.—In an extensive series of experiments, the details of which are not published in these pages, it was found that strychnin poisoning did not yield to excessive bleeding and transfusion. This was probably due to the strychnin forming a loose chemical combination with the fixed tissues of the body.

In order to test the value of bleeding and transfusion in toxemia a number of observations were made with diphtheria toxin. Animals which had received injections of diphtheria toxin were bled and transfused at the onset of the symptoms, about twenty-four hours after the injection, and were no more likely to recover than control animals which received the toxin but which were not bled and transfused. On gradually reducing the times of treatment to sixteen, twelve, eight, four, and two hours, respectively, after the injection, it was found that even in these periods of time, before symptoms appeared, the influence was negative. In as short a time as one half hour after the injection some benefit resulted. It was evident that in these cases as well as those of strychnin poisoning there was a loose chemical combination with the fixed tissues, and that when this fixation had once occurred it was not affected by bleeding and transfusion.

CHAPTER IX

THE EFFECT OF TRANSFUSION ON THE NITROGENOUS METABOLISM OF DOGS

(This research was made by Dr. H. D. Haskins, H. M. Hanna Research Fellow in the Physiological Laboratory, Western Reserve University, and published by him in the Journal of Biological Chemistry.[1]

Methods.—The dogs were put on a uniform diet, consisting of milk (230–265 c.c.) and dog biscuit, the amount given being proportionate to the body weight. A quantity of the dog biscuit sufficient for all the experiments was ground up, and after being thoroughly mixed was kept in a large bottle. Analysis of samples of this showed 3.3 per cent of nitrogen.

It will be observed from the tables that the dogs were practically in nitrogenous equilibrium before the operations took place. The dogs were kept in a large metabolism cage and were catheterized every twenty-four hours.

As to the methods of analysis of the urine, Kjeldahl's method was used for total nitrogen, while Folin's methods were used for estimating urea, ammonia, uric acid, and creatinin. Inasmuch as access to a suitable apparatus could not be had, Dr. Folin himself kindly made the creatinin estimations.

Consideration of Results.—*Experiment 1:* Dog A (see Table I) was put on the milk and biscuit diet until the nitrog-

---

[1] The transfusions were performed by the author and Drs. C. H. Lenhart, and F. W. Hitchings, all the remainder of the work being done by Dr. Haskins.

TABLE I. DOG A.

Urine No.	Date, 1907.		Volume of Urine, cc.	Nitrogen in Urine, grams.	Urea Nitrogen, grams.	Ammonia Nitrogen, grams.	In Per Cent of Total Nitrogen—		Uric Acid, grams.	Creatinin, grams.	Remarks.
							Urea N	NH_3N			
1	Jan.	14	123	3.577		.182		5.0			Milk and biscuit diet.
3	"	16	145	2.037		.102		5.0			
5	"	18	135	2.226		.051		2.2			
9	"	22	195	2.835		.134		4.7			
11	"	24	140	2.254		.108		4.8			Weight, 6.6 kg.
13	"	27	217	2.317	1.884	.062	81.3	2.6	.020		2.2 gm. nitrogen in food.
14	"	29	290	2.461	2.075	.067	84.3	2.7	.020	.171	
15	"	30	340	2.730	2.246	.078	82.2	2.8	.027	.167	Weight, 6.5 kg.
16	"	31	160	2.051		.056		2.7	.020		
17	Feb.	1	135	2.107	1.791	.050	85.0	2.4	.020	.150	Control operation, anesthesia 1 hr.
18	"	2	150	2.506		.075		3.0		.165	
19	"	3	150	2.352	1.989	.098	84.2	4.1	.022	.150	
	"	4									Transfusion; 250 cc. blood drawn; 230 c.c. blood transfused from B.
20	"	5	168	3.160	2.428	.071	76.8	2.2	.026	.162	
21	"	6	100	2.695	2.114	.112	78.3	4.1		.160	
22	"	7	140	2.905	2.625	.112	90.5	3.8	.019	.175	Weight, 6.1 kg.
23	"	8	145	2.765	2.124	.137	76.8	4.9	.020	.170	Wound suppurating.
26	"	13	175	2.730		.066		2.4	.018		Wound healthy, 2.5 gm. nitrogen in food.
28	"	16	154	2.807		.083		2.9	.022		
29	"	18	285	3.724	3.184	.134	85.0	3.6	.025	.160	Weight, 5.7 kg.
30	"	19	200	3.250	2.788	.043	85.7	1.3	.028	.144	
	"	19									Operation—hemorrhage 130 cc. blood drawn.
31	"	20	120	3.591	2.891	.070	72.0	1.9	.032	.140	
32	"	21	181	4.410	3.275	.106	74.2	2.4	.028	.142	
33	"	22	105	3.220		.104		3.2			Wound healthy.
34	"	23	125	2.780	2.313	.109	71.8	3.9		.136	
36	"	27	160	2.597		.087		3.3	.023	.142	Weight, 5.6 kg.

Table II. DOG B.

Urine No.	Date, 1907.	Volume of Urine, cc.	Nitrogen in Urine, grams.	Urea Nitrogen, grams.	Ammonia Nitrogen. grams.	In Per Cent of Total Nitrogen— Urea N	In Per Cent of Total Nitrogen— NH_3N	Uric Acid, grams.	Creatinin, grams.	Remarks.
1	Feb. 5		6.818	5.754	.308	81.0	4.5			On meat diet before operation; lost 250 c.c. blood transfused into A.
2	" 6		4.774		.252		5.2			Weight, 13 kg.

Table III. DOG C.

Urine No.	Date, 1907.	Volume of Urine, cc.	Nitrogen in Urine, grams.	Ammonia Nitrogen, in grams.	In Per Cent of Total Nitrogen.	Uric Acid, grams.	Creatinin in grams.	Remarks.
1	March 2		2.842	.087	3.0		.175	Has been on milk and biscuit diet several days; 2.73 gm. nitrogen in food.
2	" 4	190	2.310	.073	3.1	.026	.143	Weight, 6.5 kg.
3	" 5	165	2.492	.073	1.6	.027	.146	
	" 5							Operation—hemorrhage followed by transfusion from D.
4	" 6	170	3.268	.056	1.7	.033	.153	
5	" 7	200	3.255	.142	4.3	.024	.155	
6	" 8		2.328	.138	5.9			
7	" 9	85	2.247	.078	3.4	.021	.139	
8	" 11	140	2.527	.083	3.2			

Table IV. DOG D.

1	March 2	65	2.380	.048	2.0	.019	.148	Has been on milk and biscuit diet several days; 2.47 gm. nitrogen in food.
2	" 5	105	2.156	.108	5.0	.109	.130	Weight, 5.5 kg.
3	" 5							Operation—Gave blood transfused into C.
4	" 8	112	2.520	.073	2.8	.020	.154	Could not collect urine for several days.
	" 9	76	2.24	.095	4.2	.024	.146	

enous excretion had become constant, when a control operation was performed. In this, the dog was kept under ether for one hour, during which time the femoral blood vessels were exposed but not injured. This operation resulted in a slight

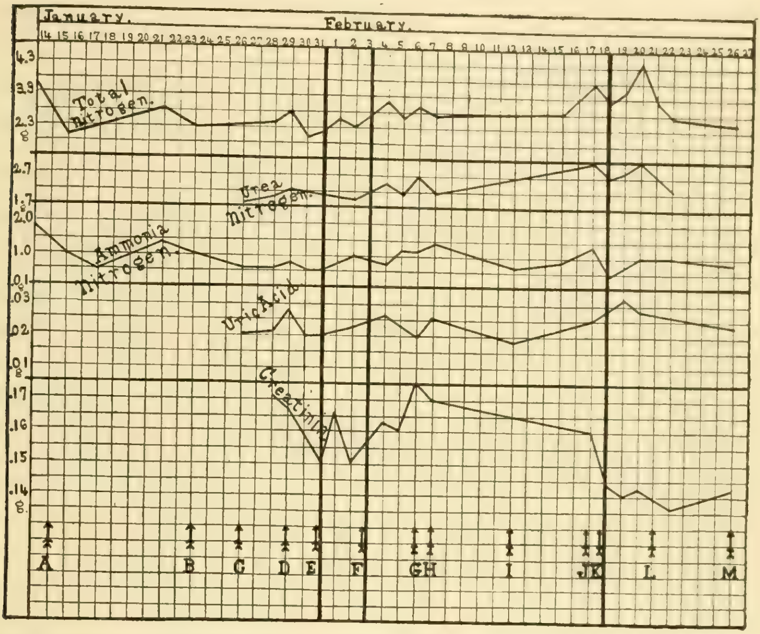


FIG. 33*a*.—THE EFFECTS OF BLEEDING AND TRANSFUSION ON THE METABOLISM OF DOGS. DOG A. A. Animal on milk and biscuit diet. B. Weight of animal, 6.6 kilos. C. 2.2 grams nitrogen in food. D. Weight, 6.5 kilos. E. Control operation (an artery was exposed just as it was when the dog was bléd and transfused), duration of anesthesia 1 hour. F. Bled 250 c.c., transfused 230 c.c. G. Weight, 6.1 kilos. H. Wound in neck suppurating. I. Wound healthy, 2.5 grams nitrogen in food. J. Weight, 5.7 kilos. K. 130 c.c. blood withdrawn. L. Wound healthy. M. Weight, 5.6 kilos. (See Table I.)

increase in the excretion of total nitrogen and some increase of that of ammonia. A few days later a transfusion was performed, 250 c.c. of blood being withdrawn and being replaced immediately afterwards by 230 c.c. from Dog B. The latter

dog had not been given the preparatory diet, but was taken from the dog room to replace the dog that had been specially dieted for this purpose but was accidentally killed. Even after allowing for body weight and for the effect of hemorrhage, Dog B was shown, by the urines following operation (Table II) to be on a distinctly higher plane of excretion than Dog A as regards total nitrogen, ammonia, uric acid, and creatinin. There was a marked change in the composition of the urine of Dog A after transfusion; namely, an increase affecting total nitrogen and urea.

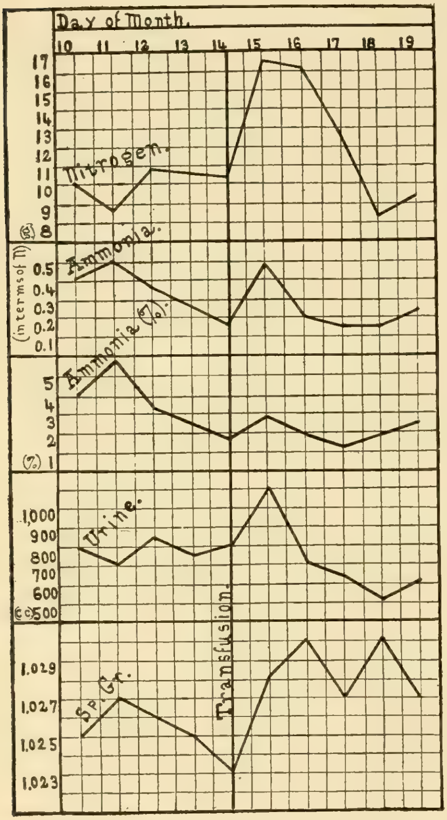


FIG. 33*b*.—THE EFFECTS OF BLEEDING AND TRANSFUSION ON THE METABOLISM OF MAN. CASE NO. IX, 10 (6,663). (See page 459.)

It might be supposed that this change was due to the character of the blood received. To decide this it was necessary to compare the above effect with that of hemorrhage alone. When the wounds had healed sufficiently and the composition of the urine had come back almost to what it was before transfusion, another operation was performed in which 130 c.c. of blood were removed.

On comparing the effect of hemorrhage (+ anesthesia) with the effect of transfusion alone in the same dog the following facts are noted:

As regards nitrogen excretion, averaging two days before and two after operation, hemorrhage caused 14.7 per cent increase, transfusion 20 per cent; as regards the per cent of nitrogen present as ammonia, averaging four days before and after, hemorrhage caused an increase amounting to 11 per cent, transfusion 15 per cent; as regards the per cent of nitrogen excreted as urea, a more marked decrease occurred from hemorrhage alone—dropping from 85.7 per cent to 72 per cent—than from transfusion, which caused a drop from 84.2 per cent to 76.8 per cent. Uric acid was increased for one day in both cases, being 18 per cent higher after transfusion and 14 per cent after hemorrhage, as compared with the day before operation. Creatinin decreased 7.8 per cent after hemorrhage, and increased 3.7 per cent (averaging several estimations before and after) after transfusion. This increase of creatinin does not seem to be at all proportional to the very high excretion of the donor (Dog B).

The effect of hemorrhage in increasing total nitrogen excretion had been previously observed by Hawk and Gies.[1]

Experiment 2: In this case both dogs (see Tables III and IV) were under exactly the same dietary conditions and their excretions were just about the same, when allowance is made for the difference in body weight. The amount of blood drawn and transfused was not determined.

Unfortunately the effect of hemorrhage on the excretion of Dog D could not be studied very successfully because accidents prevented the collecting of the urine for two days after the operation.

---

[1] Hawk and Gies: The Influence of External Hemorrhage. *Amer. Journ. of Physiol.*, xi, p. 171.

With Dog C, transfusion caused 35 per cent increase of nitrogen (averaging two days before and after operation), 48 per cent increase of ammonia nitrogen per cent (averaging three days before and after), 22 per cent increase of uric acid, and 6.5 per cent increase of creatinin (averaging two days before and after).

By comparing with Experiment 1, it is found that the increases are greater in the case of C than in that of A. Therefore, it cannot be argued that the blood of the higher (meat) diet dog, B, produced any characteristic effect different from that produced by the blood of the medium diet (milk and biscuit) dog, D. Diet does not seem to be an essential factor. Judging from the results in these two experiments, it would seem that transfusion (or rather hemorrhage followed by transfusion) produces practically the same effect on nitrogenous metabolism as does moderate hemorrhage alone, but to a much greater degree, and further, that the nature of the diet given the donor previous to transfusion is of no importance in influencing the result.

A third transfusion was successfully performed, but unfortunately the dog refused food and was quite sick following the operation, so that further work on the urines was rendered valueless.

In the case of all the other dogs, transfusion and hemorrhage were quickly recovered from, in so far as could be judged by their appearance and behavior.

Conclusions.—The work reported here is hardly extensive enough to warrant the drawing of any conclusions further than that transfusion of blood following hemorrhage has practically the same effect on nitrogenous metabolism as hemorrhage alone has. In other words, the transfusion of normal blood after hemorrhage does not prevent the effect on nitrogenous metabolism of hemorrhage alone.

CHAPTER X

TRANSFUSION AFTER BILATERAL NEPHRECTOMY

In collaboration with Dr. H. P. Cole.

EXPERIMENT 1

FEBRUARY 13, 1907.

Black mongrel dog; weight, 15 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted one hour and fifteen minutes. The dog made a good recovery.

FEBRUARY 14.

The dog vomited on taking milk forty-eight hours after the operation. He was quite weak and unable to walk steadily.

Death occurred between fifty-two and sixty-six hours after the operation (average, fifty-nine hours).

Autopsy.—The wound was clean, but there was no evidence of healing. There was bilateral subperitoneal hemorrhage.

EXPERIMENT 2

FEBRUARY 16, 1907.

Mongrel dog; weight, 12 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted one hour and twenty minutes. The dog made a good recovery.

FEBRUARY 18.

He was listless, weak, and vomited, and had an increasing temperature. Death occurred (average time) at fifty-nine hours.

Autopsy.—The operation wounds had not united. The peritoneum showed an old subperitoneal hemorrhage.

EXPERIMENT 3

FEBRUARY 23, 1907.

White mongrel dog; weight, 9.9 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The

anesthesia lasted one hour and thirty minutes. An accidental hemorrhage of 200 c.c. occurred from the renal artery. The dog made a good recovery.

FEBRUARY 24.

The general condition was good. There was no vomiting and no increase in temperature, and he was able to walk quite steadily.

FEBRUARY 25.

Sixty-eight hours after the operation he showed marked twitching of the muscles of the legs, and vomited on drinking water.

Death suddenly occurred at seventy-two hours.

Autopsy.—The wounds were clean. Healing had not occurred. The peritoneum showed old subperitoneal hemorrhage.

EXPERIMENT 4

MARCH 4, 1907.

Coach dog; weight, 15 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted one hour. The dog made a good recovery.

MARCH 6.

Vomiting occurred fifty hours after the operation.

Death occurred (average time) fifty-nine hours after the operation.

Autopsy.—The wounds were clean. There was no healing. An old subperitoneal hemorrhage was found.

EXPERIMENT 5

MARCH 14, 1907.

Black and tan dog; weight, 10 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted one hour. The dog made a good recovery.

MARCH 15.

The dog was in good condition.

MARCH 16.

Death occurred forty-four hours after the operation. The dog was in fair condition two hours before death.

Autopsy.—The wounds were healthy. There was no healing. An old bilateral subperitoneal hemorrhage was found.

BILATERAL NEPHRECTOMY AND TRANSFUSION

EXPERIMENT 1

FEBRUARY 18, 1907.

Mongrel dog; weight, 8.8 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted one hour.

FEBRUARY 19.

The sutures suppurated out of the left skin wound.

FEBRUARY 20.

There was frequent vomiting forty-eight hours after the operation.

At this time under ether anesthesia (duration, one hour and fifty minutes) the dog was bled 100 c.c. and transfused rapidly for ten minutes from another dog. The anastomosis was made by the cannula method from a branch of the carotid artery of the donor to the femoral vein of the recipient in this and all the other experiments of this series.

FEBRUARY 21.

The dog was very weak and listless, and refused nourishment.

FEBRUARY 22.

Death occurred forty-four hours after the transfusion, and ninety-two hours after the nephrectomy.

EXPERIMENT 2

FEBRUARY 25, 1907.

White mongrel dog; weight, 8 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted one hour and fifteen minutes. The dog made a good recovery.

FEBRUARY 26.

The dog was in excellent condition.

FEBRUARY 27.

The dog was in fair condition. There was some twitching of the muscles.

February 28.

The legs twitched, and vomiting occurred on drinking.

Seventy-two hours after the nephrectomy, while under ether (duration, one hour and forty-five minutes), the dog was bled 200 c.c. and transfused rapidly for seven minutes from another dog. The anastomosis was made by the cannula method.

March 1.

The dog was listless and weak, and vomited.

Death occurred forty hours after the transfusion, and one hundred and twelve hours after the nephrectomy.

EXPERIMENT 3

March 7, 1907.

Black and tan dog; weight, 13 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted fifty minutes.

March 8.

The dog was in fair condition, but weak.

March 9.

The dog was very weak.

Forty-eight hours after the nephrectomy, under ether anesthesia (duration, one hour and forty-five minutes), the dog was bled 200 c.c., and transfused rapidly for ten minutes from another dog. The anastomosis was made by the cannula method.

March 10.

Death occurred eighteen hours after the transfusion, and sixty-six hours after the nephrectomy.

Autopsy.—The wounds were unhealed.

EXPERIMENT 4

March 11, 1907.

Coach dog; weight, 12 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted fifty minutes.

March 12.

The dog was weak, and vomited on taking liquids.

MARCH 13.

Forty-eight hours after the nephrectomy, under ether anesthesia (duration, one hour and fifty minutes), the dog was bled 175 c.c., and transfused rapidly for seven minutes from another dog. The anastomosis was by the cannula method.

Death occurred eighteen hours after the transfusion, and sixty-six hours after the nephrectomy.

Autopsy.—The wounds were unhealed.

EXPERIMENT 5

MARCH 16, 1907.

Bull terrier bitch; weight, 9 kilos. Under ether anesthesia a bilateral nephrectomy was performed by the posterior route. The anesthesia lasted fifty minutes. The dog made a good recovery.

MARCH 17.

The dog was weak.

MARCH 18.

The dog was in fair condition. She vomited.

Forty-eight hours after the nephrectomy, under ether anesthesia (duration, one hour and fifty minutes), the dog was bled 150 c.c., and transfused rapidly for ten minutes from another dog.

MARCH 19.

The dog was very weak, and refused nourishment.

Death occurred forty-two hours after the transfusion, and ninety hours after the nephrectomy.

Autopsy.—The wounds were not healed. The peritoneum was clear.

TABLE I

BILATERAL NEPHRECTOMY WITHOUT TRANSFUSION

Experiment	Time under Ether	Duration of Life after Nephrectomy
1	1 hr., 15 min.	59 hrs.
2	1 " 20 "	59 "
3	1 " 30 "	72 "
4	1 " 0 "	59 "
5	1 " 0 "	44 "
Average		58 "

TABLE II

BILATERAL NEPHRECTOMY WITH SUBSEQUENT TRANSFUSION

Experiment	Time Under Ether—		Amount of Blood Transfused	Duration of Transfusion	Time of Transfusion after Nephrectomy	Duration of Life—	
	I During Nephrectomy	II During Transfusion				I After Transfusion	II After Nephrectomy
1	1 hr., 0 min.	1 hr., 50 min.	100 c.c.	10 min.	48 hrs.	44 hrs.	92 hrs.
2	1 " 15 "	1 " 45 "	200 "	7 "	72 "	40 "	112 "
3	50 "	1 " 45 "	200 "	10 "	48 "	18 "	66 "
4	50 "	1 " 50 "	175 "	7 "	48 "	18 "	66 "
5	50 "	1 " 50 "	150 "	10 "	48 "	42 "	90 "
Average						32 "	85 "

GENERAL SUMMARY

THE object of these experiments was to ascertain whether transfusion would prolong the life of dogs beyond the normal period of survival after bilateral nephrectomy. The experiments were divided into two series. In the first bilateral nephrectomy alone was performed, and in the second it was performed and followed by transfusion at a time as nearly before death would have been expected to have occurred as it was possible to determine and yet leave a margin of safety.

In the first series of experiments on the 5 dogs on which transfusion was not performed, the longest duration of life was seventy-two hours and the shortest forty-four hours. This compares favorably with the duration of life in the dogs operated on by Vitzou, his maximum survival being seventy-one hours. Vitzou obtained a length of life of one hundred and nine, one hundred and forty-two, one hundred and forty-six, and one hundred and sixty-four hours' duration in dogs which had received injections of serum from blood from the renal vein. He naturally concluded that the serum acted favorably,

and was a vehicle of the internal secretion of the kidney. Chatin and Guinard, however, had one dog that lived one hundred and twenty-four hours, and Lavis had a dog that lived one hundred and forty-one hours, but no mention is made as to whether or not they received special treatment. Lavis mentions another dog which lived one hundred and sixty-two hours, and which only received injections of physiological saline solution. He concluded that the variation of survival depends on a complex idiosyncrasy—the age of the dog, the quantity of water absorbed, and the state of the digestive tract playing the chief rôles. He also said that the animals which lived the longest were the ones which received the greatest amount of fluid.

The dogs utilized were apparently healthy. They were of various ages and weights, and did not have any special routine treatment. They received milk and water as they would ordinarily have received it in the dog house. There appeared to be no connection between the age and weight of the individual dog and the length of time which it survived.

All of the dogs were under ether anesthesia for at least an hour, and 1 was under for one hour and thirty minutes. Nearly all showed symptoms of nausea and vomiting, and these were the only symptoms which might be called uremic.

One dog survived the operation forty-four hours, 3 about fifty-nine hours, and 1 seventy-two hours. Averaging these figures the duration was fifty-eight hours and thirty-six minutes.

In the second series, as in the first, the operation was performed on 5 dogs. The general conditions were the same. All were transfused forty-eight hours after the nephrectomy, with the exception of 1 which was transfused at the end of the seventy-second hour. At the time the nephrectomy was done 3 were under ether fifty minutes, 1 one hour, and 1 one hour

and fifteen minutes. At the time the transfusion was done 3 were under ether one hour and fifty minutes and 2 one hour and forty-five minutes.

The anastomosis was made between either the internal or the external branch of the common carotid artery of the donor and the femoral vein of the recipient (the nephrectomized dog). The recipient was bled either from the femoral vein or from the carotid artery. Two dogs were bled 200 c.c. each; 1, 175; 1, 150; and 1, 100 c.c. before beginning to transfuse.

Of the 4 dogs which were transfused forty-eight hours after the nephrectomy, 1 died in forty-four hours after the transfusion, 1 in forty-two hours, and 2 in eighteen hours. The dog which was transfused seventy-two hours after the nephrectomy died forty hours after the transfusion. Of the first four dogs, 2 died ninety hours after the nephrectomy, and 2 sixty-six hours. The seventy-two-hour dog died one hundred and twelve hours after the nephrectomy. The average time of survival after nephrectomy and transfusion was eighty-five hours and twelve minutes.

Apparently, therefore, transfusion slightly prolonged the lives of nephrectomized dogs. Comparing these results with those obtained by the previously mentioned investigators, it must be concluded that under these circumstances transfusion has no material effect.

CHAPTER XI

TRANSFUSION AFTER ILLUMINATING GAS POISONING

In collaboration with Dr. C. H. Lenhart.

PROTOCOLS OF EXPERIMENTS

EXPERIMENT 1

Illuminating Gas Poisoning; Bleeding and Transfusion; Recovery

NOVEMBER 20, 1906.

Donor.—Mongrel dog; weight, 4.5 kilos; condition, good. *Recipient.*—Young mongrel bitch; weight, 4 kilos; condition, good. The blood-pressure of the recipient was recorded on a drum in the usual way, and a cannula was inserted in a femoral artery for bleeding. A carotid artery of the donor was anastomosed to a femoral vein of the recipient by the suture method. Both dogs were anesthetized with ether, but with the recipient only enough was used to secure insensibility until the full effects of the gas were produced, when it was no longer necessary. The arrangements for giving the illuminating (coal) gas from the street mains is described later, and was practically the same for all the experiments. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	11.43	102 mm.	This control showed the normal blood pressure.
2	11.45	108 mm.	The reflexes were active.
	11.46		The gas was turned on.
3	11.47	102 mm.	The eye reflexes were lost. The breathing was labored.
4	11.49	98 mm.	
5	11.50	4 mm.	Turned off the gas. Duration of flow, four minutes. The respiration stopped, and the circulation also in a few seconds. Began to bleed, started the transfusion, manipulated the heart through the chest wall, and began artificial respiration.
	11.55		Stopped the artificial respiration and manipulation.
6	11.55½	80 mm.	
7	11.58	94 mm.	

Control	Time	Blood-Pressure	Remarks
	11.59		Stopped the bleeding. Total duration, nine minutes.
8	12.12	92 mm.	Stopped the transfusion. Total duration, twenty-two minutes.
9	12.14	78 mm.	Removed a clot from the carotid cannula.
10	12.16½	84 mm.	
11	12.24	78 mm.	
12	12.40	88 mm.	
13	1.42	80 mm.	
14	1.45	76 mm.	
15	2.12	75 mm.	Two hours after the transfusion.
16	2.19	62 mm.	Removed another clot.
	2.20½		Turned on the gas again.
17	2.21⅓	58 mm.	The respiration and circulation stopped.
18	2.23	2 mm. (?)	Began to manipulate the heart and give artificial respiration.
19	2.29	26 mm.	The heart beat again. Stopped the manipulation. Maintained the artificial respiration. There was an occasional spasmodic respiratory gasp.
20	2.32	33 mm.	Spontaneous respiration began eleven minutes after respiration ceased.
21	2.47	44 mm.	
22	3.00	42 mm.	
23	3.15	36 mm.	Killed both dogs.

Summary.—Inhalation of illuminating gas by a dog for four minutes caused cessation of respiration and circulation, with a fall in the blood-pressure to 4 mm. On bleeding freely, giving artificial respiration, compressing the heart through the chest wall, and transfusing for twenty-two minutes, the blood-pressure was brought back to 94 mm., and the circulation and respiration were resumed. By the end of two hours the pressure had only fallen to 75 mm. The experiment was then repeated, with a fall in pressure to 2 mm., a return to a maximum of 44 mm., with spontaneous respiration and circulation, and maintenance of a pressure of 36 mm. or more until the dog was killed twenty-eight minutes later.

EXPERIMENT 2

Illuminating Gas Poisoning; Cessation of Circulation and Respiration for Two Minutes; Bleeding and Transfusion; Death

Donor.—Young mongrel dog; weight, 7.2 kilos; condition, fair. *Recipient.*—Mongrel dog; weight, 4 kilos; condition, fair. Ether anesthesia for both dogs. All the other arrangements were as in Experiment 1 of this series. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	12.07	128 mm.	Turned on the gas.
	12.08½		
2	12.11½	126 mm.	
3	12.15¼	106 mm.	
4	12.25	114 mm.	
5	12.25½	98 mm.	The eye reflexes had disappeared.
6	12.27	88 mm.	
7	12.27½	60 mm.	There was an occasional respiratory spasm.
	12.29		
8	12.30	32 mm.	
9	12.30¼	30 mm.	
10	12.30½	20 mm.	
11	12.31	10 mm.	
12	12.32½	6 mm.	Turned off the gas. Duration of flow, twenty-four minutes. The respiration and circulation stopped. Began to bleed.
13	12.34½	10 mm.	Owing to trouble in getting the transfusion started two minutes were lost before the flow began, and before artificial respiration and manipulation of the chest were begun at this time.
	12.39		Stopped bleeding. Duration, six and a half minutes.
14	12.42	20 mm.	The recipient died. The donor was killed.

Summary.—Inhalation of illuminating gas by a dog for twenty-four minutes caused complete cessation of respiration and circulation, with a fall in blood-pressure to 6 mm. Attempts at resuscitation by means of transfusion and artificial respiration failed.

EXPERIMENT 3

Illuminating Gas Poisoning; Bleeding and Transfusion; Recovery

NOVEMBER 22, 1906.

Donor.—Mongrel bitch; weight, 5.8 kilos; condition, good. *Recipient.*—Mongrel dog; weight, 10.8 kilos; condition, good. Ether anesthesia for both dogs. All the other arrangements were as in Experiment 1 of this series. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	2.39	144 mm.	
2	2.45	150 mm.	Turned on the gas.
3	2.48½	140 mm.	
4	2.49¼	124 mm.	
5	2.50	112 mm.	
6	2.51½	18 mm.	The eye reflexes were lost.

Control	Time	Blood-Pressure	Remarks
	2.52½		Turned off the gas. Duration of flow, seven and a half minutes. The respiration and circulation stopped. Began transfusion, bleeding, manipulation of heart, and artificial respiration.
	2.54		Irregular heart beats began, but no respiration.
7	2.57	80 mm.	Spontaneous respiration began at the rate of 20 per minute.
8	2.59	100 mm.	
9	3.01	112 mm.	Stopped the transfusion and the bleeding. Duration of each, eight and one-half minutes.
10	3.06	122 mm.	
11	3.22	108 mm.	
12	3.36	110 mm.	
13	3.47	118 mm.	Killed both dogs.
14	4.01	108 mm.	

Summary.—Inhalation of illuminating gas by a dog for seven and a half minutes caused complete cessation of respiration and circulation, with a fall in blood-pressure to 18 mm. Then simultaneous bleeding, transfusion, artificial respiration, and rhythmic pressure on the chest brought back spontaneous respiration and circulation, and raised the blood-pressure to a maximum of 122 mm. The pressure was maintained up to 108 mm. or more for one hour, when the dog was killed.

EXPERIMENT 4

Illuminating Gas Poisoning; Attempted Resuscitation without Bleeding or Transfusion; Death

November 23, 1906.

Dog; weight, 7.2 kilos; condition, good. Ether anesthesia. Gas was given as in the other experiments.

Control	Time	Blood-Pressure	Remarks
1	1.00	148 mm.	
2	1.01	134 mm.	
	1.01¼	135 mm.	Turned on the gas.
3	1.03½	135 mm.	
4	1.04½	130 mm.	
5	1.07	110 mm.	
6	1.07½	94 mm.	
	1.08½		The respiration stopped.
7	1.11½	70 mm.	Turned off the gas. Duration of flow, ten and a quarter minutes.
8	1.20¼	8 mm.	Rhythmic pressure on the heart and chest.
9	1.26	6 mm.	
10	1.35	4 mm.	Stopped the manipulation. Duration, fifteen minutes. Death occurred.

Summary.—Inhalation of illuminating gas by a dog for ten and a quarter minutes caused complete cessation of respiration and circulation, with a fall in the blood-pressure to 8 mm. Rhythmic pressure on the heart and chest for fifteen minutes failed to bring about resuscitation.

EXPERIMENT 5

Illuminating Gas Poisoning; Bleeding and Transfusion; Recovery

NOVEMBER 24, 1906.

Donor.—Mongrel bitch; weight, 9.9 kilos; condition, good. *Recipient.*—Mongrel bitch; weight, 7.2 kilos; condition, good. Ether anesthesia for both dogs. All the other arrangements were as in Experiment 1 of this series. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	2.03	124 mm.	
	2.04½		Turned on the gas.
2	2.07½	128 mm.	
3	2.09	120 mm.	
4	2.12	118 mm.	
5	2.16	102 mm.	The eye reflexes were lost.
	2.18	12 mm.	The respiration and circulation both stopped. Turned off the gas. Duration of flow, fourteen minutes. Began to bleed, transfuse, press rhythmically upon the chest over the heart, and give artificial respiration. The heart began to beat again in a few seconds.
6	2.19	104 mm.	Began to breathe spontaneously.
7	2.20	124 mm.	Stopped bleeding and transfusing. Duration of each, two minutes.
8	2.21	138 mm.	
9	2.22	152 mm.	
10	2.30	158 mm.	
11	2.32	174 mm.	
12	2.33½	164 mm.	
13	2.35	158 mm.	
14	2.47	152 mm.	
15	3.04	148 mm.	
16	3.15	149 mm.	
17	3.20	148 mm.	
18	3.30	134 mm.	Both dogs killed.

Summary.—Inhalation of illuminating gas by a dog for fourteen minutes caused complete cessation of respiration and circulation, with a fall in the blood-pressure to 12 mm. Then simultaneous

bleeding, transfusion, artificial respiration, and rhythmic pressure on the heart and chest brought back spontaneous circulation and respiration, and raised the blood-pressure to a maximum of 174 mm. (50 mm. higher than the original level). A level higher than the original level was maintained for one hour and ten minutes, when the dog was killed. (See Fig. 34.)

EXPERIMENT 6

Illuminating Gas Poisoning; Attempted Resuscitation without Bleeding or Transfusion; Death

NOVEMBER 26, 1906.

Dog; weight, 10.8 kilos; condition, good. Ether anesthesia. Gas was given as in the other experiments.

Control	Time	Blood-Pressure	Remarks
1	11.40	150 mm.	
	11.49		Turned on the gas.
2	11.51	144 mm.	
3	11.52	44 mm.	The respirations stopped.
4	11.54	8 mm.	The circulation stopped. Turned off the gas. Duration of flow, five minutes in all (three minutes until the respiration stopped). The chest was then rhythmically compressed for fifteen minutes without bringing about resuscitation.

Summary.—Inhalation of illuminating gas by a dog for five minutes (the last two of the five minutes being after all respiration had ceased) caused complete cessation of respiration and circulation, with a fall in blood-pressure to 8 mm. Rhythmic pressure on the heart and chest for fifteen minutes failed to bring about resuscitation or to raise the blood-pressure.

EXPERIMENT 7

Illuminating Gas Poisoning; Bleeding and Transfusion; Death

DECEMBER 4, 1906.

Donor.—Mongrel dog; weight, 9 kilos; condition, good. *Recipient.*—Mongrel bitch; weight, 7.2 kilos; condition, good. Ether anesthesia for both dogs. All the other arrangements were as in

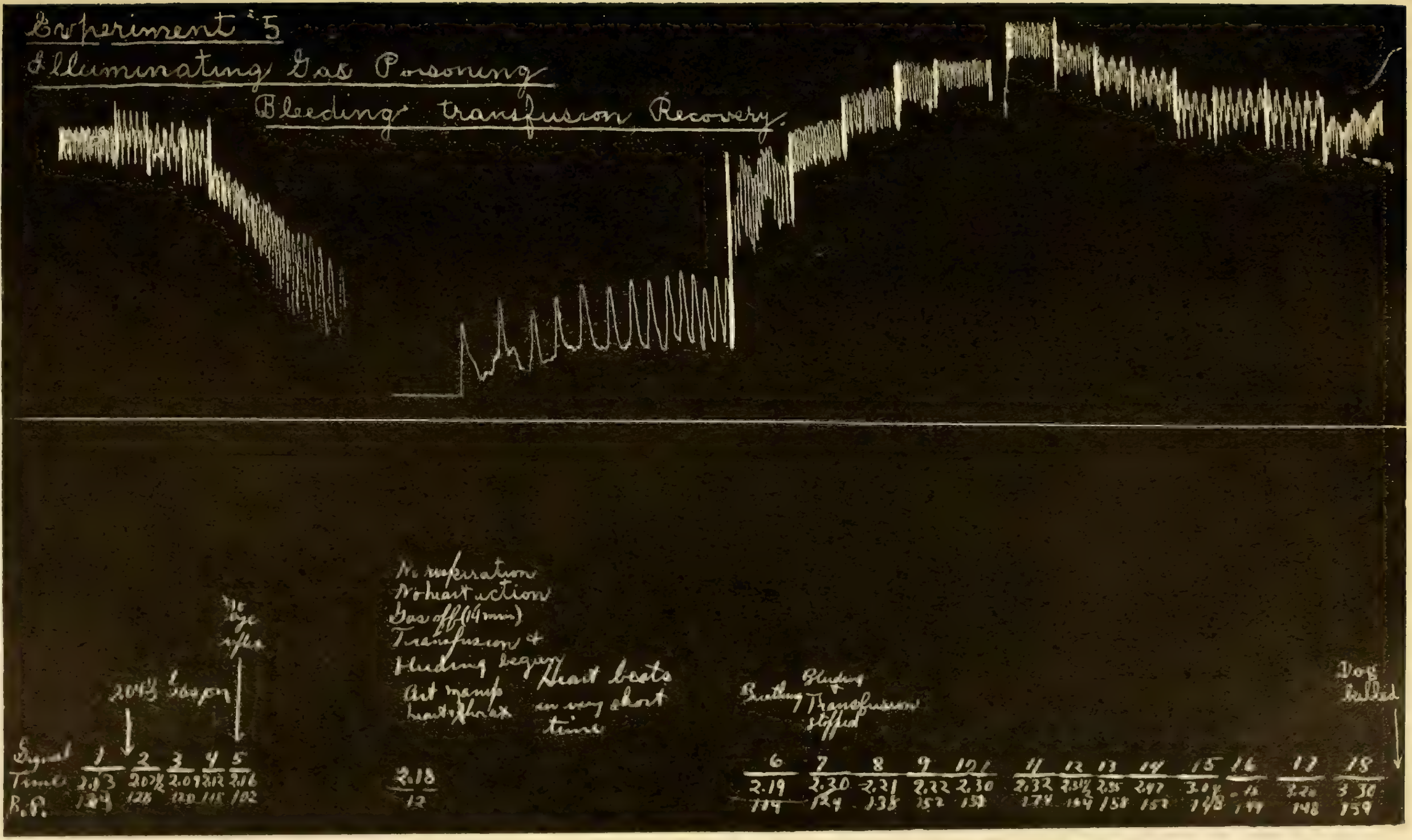


FIG. 34.—ILLUMINATING GAS POISONING, BLEEDING, TRANSFUSION, RECOVERY. The blood-pressure was raised considerably above the initial level by the transfusion, and was well sustained. (Experiment 5.)

Experiment I of this series. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	10.31	158 mm.	
2	10.31½	150 mm.	Turned on the gas.
3	10.35	140 mm.	
	10.35½		The respiration stopped.
4	10.41½		The circulation stopped. Turned off the gas. Duration of flow, ten minutes altogether (four minutes only until the respiration stopped). Began to bleed, transfuse, give artificial respiration, and to compress the heart through the thoracic wall for fifteen minutes without bringing about resuscitation. The donor was killed.

Summary.—Inhalation of illuminating gas by a dog for ten minutes (four minutes only until the respiration stopped) caused complete cessation of respiration and circulation, with a fall in the blood-pressure to the abscissa. Then simultaneous bleeding, transfusion, artificial respiration, and compression of the heart through the thoracic wall failed to bring about resuscitation or to raise the blood-pressure.

EXPERIMENT 8

Illuminating Gas Poisoning; Attempted Resuscitation with Bleeding, but without Transfusion; Death

DECEMBER 6, 1906.

Dog; weight and condition not stated. Ether anesthesia. Gas was given as in the other experiments.

Control	Time	Blood-Pressure	Remarks
1	2.42	114 mm.	Turned on the gas.
2	2.47	103 mm.	
3	2.48	96 mm.	The respiration stopped.
	2.49		
4	2.49½	31 mm.	
5	2.52½	8 mm.	The circulation almost stopped. Turned off the gas. Duration of flow, five and a half minutes (two minutes until the respiration stopped). Began to bleed, give artificial respiration, and to compress the thorax over the heart rhythmically for ten minutes without result. The dog was killed.

Summary.—Inhalation of illuminating gas by a dog for five and a half minutes (the last three and a half minutes being after all respiration had ceased) caused complete cessation of respiration and almost complete cessation of circulation, with fall of the blood-pressure to 8 mm. Continuous bleeding, artificial respiration, and rhythmic compression on the heart through the thoracic wall for ten minutes failed to bring about resuscitation.

EXPERIMENT 9

Illuminating Gas Poisoning; Bleeding and Transfusion; Death

DECEMBER 15, 1906.

Donor.—Fox terrier dog; weight, 8.1 kilos; condition, good. *Recipient.*—Fox terrier bitch; weight, 5.4 kilos; condition, good. Ether anesthesia for both dogs. All other arrangements as in Experiment 1 of this series. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	2.30	150 mm.	
	2.35		Turned on the gas.
2	2.40	150 mm.	
3	2.50	130 mm.	
4	2.51	80 mm.	Turned off the gas. Duration of flow, sixteen minutes. There was occasional spasmodic respiration which ceased in a few seconds.
5	2.55	13 mm.	The circulation stopped. Began to bleed, transfuse, give artificial respiration, and rhythmically compress the thorax. Resuscitation could not be brought about after fifteen minutes of effort.

Summary.—Inhalation of illuminating gas by a dog for sixteen minutes caused complete cessation of the respiration and circulation with fall of blood-pressure to 13 mm. Bleeding, transfusion, artificial respiration, and rhythmic compression on the heart through the thoracic wall for fifteen minutes failed to bring about resuscitation.

EXPERIMENT 10

Illuminating Gas Poisoning; Bleeding and Intravenous Infusion of Saline Solution; Death

DECEMBER 19, 1906.

Mongrel dog; weight, 6.3 kilos; condition, good. Ether anesthesia. Gas was given as in the other experiments.

Control	Time	Blood-Pressure	Remarks
1	2.49	150 mm.	
2	3.00	140 mm.	
3	3.05	136 mm.	Turned on the gas.
4	3.08	116 mm.	
5	3.12½	44 mm.	The respiration stopped.
6	3.14	10 mm.	Turned off the gas. Duration of flow, nine minutes (seven and a half minutes until the respiration stopped). The circulation had almost stopped.
7	3.14½	9 mm.	Began to bleed.
8	3.14⅔	10 mm.	Began to give saline infusion intravenously, artificial respiration, and cardiac massage through the thoracic wall.
9	3.24	10 mm.	Ten minutes of effort produced no effect. 400 c.c. of saline were given, and 200 c.c. of blood were removed.

Summary.—Inhalation of illuminating gas by a dog for nine minutes (the last one and a half minutes were after respiration had ceased) caused complete cessation of respiration, and almost complete cessation of circulation, with fall of blood-pressure to 9 mm. Bleeding, infusion of normal saline solution, artificial respiration, and rhythmic compression on the heart through the thoracic wall failed to bring about resuscitation.

EXPERIMENT 11

Illuminating Gas Poisoning; Comparison of Effects of Bleeding and Transfusion, and Bleeding and Saline Infusion in Dogs Poisoned to About the Same Degree; Recovery of Transfused Dog; Death of Infused Dog

DECEMBER 21, 1906.

Donor.—Mongrel dog; weight, 8.1 kilos; condition, good. *Recipient.*—Mongrel dog; weight, 9 kilos; condition, good. "*Saline*"

Dog.—Mongrel dog; weight, 6.3 kilos; condition, good. Ether anesthesia for all three dogs. Other arrangements for donor and recipient as in the other gas experiments.

Control	Time	Blood-Pressure		Remarks
		Recipient	"Saline" Dog	
1	2.40	142 mm.	164 mm.	
2	2.49	140 mm.	152 mm.	Turned on the gas.
3	2.50	140 mm.	136 mm.	Turned off the gas for one half minute.
	2.54			Both recipient and "saline" dog stopped breathing at practically the same time.
	2.56			Turned off the gas. Duration of flow, six minutes (four minutes until respiration of both dogs stopped). Began to bleed both, to transfuse the recipient, to infuse the "saline" dog, to give each artificial respiration, and to rhythmically compress the heart of each through the chest wall.
4	2.58½	68 mm.	30 mm.	The recipient breathed spontaneously. The "saline" dog took a few gasps for breath.
5	3.02	124 mm.	16 mm.	
6	3.07	126 mm.	19 mm.	Stopped the transfusion and the infusion. Duration of each, eleven minutes (400 c.c. of saline given).
7	3.09	134 mm.	10 mm.	
8	3.21	140 mm.		
9	3.45	144 mm.		Killed the recipient. Failed to resuscitate the "saline" dog.

Summary.—The blood-pressure of the recipient was not reduced as much as that of the "saline" dog after both had inhaled illuminating gas for the same length of time, although the respiration of each ceased at the same time. The application of the same measures to each (with the exception that one dog was transfused and the other infused with normal saline solution) resuscitated the transfused dog, but did not resuscitate the saline-infused dog.

EXPERIMENT 12

Illuminating Gas Poisoning; Bleeding and Intravenous Saline Infusion; Death

DECEMBER 23, 1906.

Mongrel dog; weight, 7.7 kilos; condition, good. Ether anesthesia. The gas was given as in the other gas experiments.

Control	Time	Blood-Pressure	Remarks
1	11.20	138 mm.	
2	11.30	106 mm.	Turned on the gas.
	11.34		Respiration stopped.
3	11.36	8 mm.	The circulation stopped. Turned off the gas. Duration of flow, six minutes (four minutes until the respiration stopped). Began to bleed, infuse saline solution into the femoral vein, give artificial respiration, and rhythmically compress the heart through the thoracic wall. Maintained these measures for fifteen minutes, but could not bring about resuscitation. 450 c.c. of saline infusion were given, and about 100 c.c. of blood were removed.

Summary.—Inhalation of illuminating gas by a dog for six minutes (the last two minutes were after respiration had ceased) was followed by complete cessation of respiration and circulation, with fall of the blood-pressure to 8 mm. Infusion of saline solution, bleeding, artificial respiration, and rhythmic pressure on the heart through the thoracic wall failed to bring about resuscitation.

EXPERIMENT 13

Illuminating Gas Poisoning; Bleeding and Transfusion; Recovery

FEBRUARY 11, 1907.

Donor.—Mongrel bitch; weight, 8.1 kilos; condition, good. *Recipient.*—Mongrel dog; weight, 7.7 kilos; condition, good. Ether anesthesia for both dogs. All the other arrangements were practically the same as in Experiment 1 of this series. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	2.25	170 mm.	
2	2.35	162 mm.	Turned on the gas.
3	2.45	156 mm.	
4	2.50	146 mm.	
5	2.53	134 mm.	
6	3.00	122 mm.	
7	3.08	114 mm.	
8	3.14	104 mm.	
9	3.21	90 mm.	
10	3.22½	74 mm.	
11	3.24	12 mm.	Turned off the gas. Duration of flow, forty-nine minutes. Respiration and circulation ceased. Began to bleed, transfuse, give artificial respiration, and rhythmically compress the heart through the thoracic wall.
12	3.25	36 mm.	
13	3.26	70 mm.	Spontaneous respiration began.
14	3.28	126 mm.	Stopped transfusing. Duration of flow, four minutes. Stopped bleeding. Amount of blood removed, 100 c.c.
15	3.30	150 mm.	
16	3.40	145 mm.	
17	3.50	142 mm.	
18	4.10	142 mm.	
19	4.30	146 mm.	
20	4.45	148 mm.	Killed both dogs.

Summary.—Inhalation of illuminating gas by a dog for forty-nine minutes was followed by complete cessation of respiration and circulation, with fall of the blood-pressure to 12 mm. Then bleeding, transfusion, artificial respiration, and rhythmic compression of the heart through the thoracic wall brought about recovery, the blood-pressure rising to a maximum of 150 mm., and only falling to 148 mm. in one and a half hours, when the dog was killed.

EXPERIMENT 14

Illuminating Gas Poisoning; Bleeding and Transfusion; Recovery

FEBRUARY 15, 1908.

Donor.—Mongrel dog; weight, 9.5 kilos; condition, good. *Recipient.*—Mongrel dog; weight, 9 kilos; condition, good. Ether anesthesia for both dogs. All the other arrangements were the same as in Experiment 1 of this series. The cannula method of making the anastomosis was used. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	10.30	102 mm.	
	10.31		Turned on the gas.
2	10.47	98 mm.	
3	10.55	90 mm.	
4	10.57	76 mm.	
5	10.58	70 mm.	
6	10.59	78 mm.	
7	11.01	68 mm.	
8	11.03	56 mm.	Respiration spasmodic.
	11.03½		Respiration ceased. Circulation almost ceased.
9	11.03¾	20 mm.	Turned off the gas. Duration of flow, thirty-two minutes. Began to bleed, transfuse, give artificial respiration, and rhythmically compress the heart through the thoracic wall.
10	11.07	62 mm.	Spontaneous respiration established. Stopped the bleeding.
	11.10		Stopped the transfusion. Duration of flow, six and a quarter minutes.
11	11.12½	134 mm.	
12	11.25	125 mm.	
13	11.30	124 mm.	
14	11.40	118 mm.	
15	11.50	110 mm.	
16	12.55		Killed both dogs.

Summary.—Inhalation of illuminating gas by a dog for thirty-two minutes was followed by complete cessation of respiration, and almost complete cessation of circulation, with fall of the blood-pressure to 20 mm. Then bleeding, transfusion, artificial respiration, and rhythmic compression of the heart through the thoracic wall brought about recovery, with maintenance of a blood-pressure of 110 mm. or over (maximum, 134 mm.) for five hours and thirty-three minutes, when the dog was killed.

EXPERIMENT 15

Illuminating Gas Poisoning; Bleeding and Transfusion; Recovery

February 14, 1907.

Donor.—Mongrel bitch; weight, 8.1 kilos; condition, good. *Recipient.*—Mongrel dog; weight, 9 kilos; condition, good. Ether anesthesia for both dogs. Other arrangements as in Experiment 1 of this series. All data refer to the recipient, unless otherwise specified.

Control	Time	Blood-Pressure	Remarks
1	12.11	145 mm.	
	12.15		Turned on the gas.
2	12.30	140 mm.	
3	12.45	138 mm.	
4	12.54	126 mm.	
5	12.56	112 mm.	
6	12.57	102 mm.	
7	12.59	96 mm.	
8	1.03	84 mm.	
9	1.04½	76 mm.	
10	1.06	20 mm.	The respiration stopped. Turned off the gas. Duration of flow, fifty-one minutes. Began to bleed, transfuse, give artificial respiration, and rhythmically compress the heart through the thoracic wall. The circulation had not quite stopped.
11	1.09	22 mm.	Heart beating faintly.
12	1.11	30 mm.	There were a few gasping respirations.
13	1.12	36 mm.	Heart beating well.
14	1.14	28 mm.	Spontaneous respiration established.
15	1.15	66 mm.	Stopped the transfusion. Duration of flow, nine minutes.
16	1.16	94 mm.	
17	1.19	98 mm.	The eye reflexes were restored.
18	1.25	113 mm.	
19	1.32	124 mm.	
20	1.41	116 mm.	
21	2.10	123 mm.	
22	2.30	95 mm.	Killed both dogs.

Summary.—Inhalation of illuminating gas by a dog for fifty-one minutes caused complete cessation of respiration, and almost complete cessation of circulation, with fall of the blood-pressure to 20 mm. Then bleeding, transfusion, artificial respiration, and rhythmic compression of the heart through the thoracic wall brought about recovery, with maintenance of blood-pressure of 95 mm. or more (the maximum was 124 mm.) for one hour and fourteen minutes, when the dog was killed.

GENERAL SUMMARY

The chief toxic factor in artificial illuminating (coal) gas poisoning is carbon monoxid. Carbon monoxid constitutes from 6 to 10 per cent of illuminating gas. It occurs in the so-called " water gas " to the extent of 30 to 40 per cent. It

is the important toxic constituent of the "after damp" of mines, and of the gas from charcoal and coal stoves and from blast furnaces.

Its action on animals is purely that of asphyxia. It combines with hemoglobin, displacing the oxygen. Its affinity for hemoglobin is three hundred times that of oxygen. The resulting compound is not perfectly stable, so that when oxygen is present in very great excess, carbonic oxid hemoglobin will be decomposed and oxyhemoglobin formed. Hence the rational treatment of patients by oxygen inhalation.

Haldane placed mice in oxygen under a pressure of two atmospheres, so that sufficient oxygen went into simple solution in the blood serum to support life independently of the hemoglobin. Sufficient carbon monoxid was present to saturate their hemoglobin completely. Under these conditions the mice remained normal as to symptoms, showing that the carbon monoxid had no direct toxic action. When the pressure was removed and the mice put out in the air they died with symptoms of asphyxia.

Haldane claims that during recovery carbon monoxid is given off from the lungs as such and is not destroyed or oxidized in the body.

To summarize the symptoms of carbon monoxid poisoning: there is stimulation of the central nervous system followed by paralysis, the order of affection of the central nervous system being brain, spinal cord, and medulla. To state them in detail:

1. There is cerebral excitement.

2. There is stimulation of the medulla: (*a*) Dilatation of the cutaneous vessels with flushing. The lips are pink. If the poisoning be very acute there may be cyanosis, due to the fact that the venous blood does not yet contain much carbon monoxid. (*b*) The blood-pressure rises, due to the stimulation

of the vasomotor center. There may be ecchymosis formation. (*c*) The heart is first slowed, due to vagus stimulation. (*d*) Respiration is dyspneic. (*e*) There may be vertigo, vomiting, and mydriasis.

3. Paralysis of the medullary centers follows: (*a*) The blood-pressure falls, due to vasomotor paralysis. (*b*) The heart rate is increased, due to vagus paralysis. (*c*) Paralysis of respiration occurs and death follows.

4. Following cerebral excitement there is unconsciousness, anesthesia, and coma.

5. There are often ascending convulsions.

6. At death the hemoglobin is usually combined with the carbon monoxid to the extent of 60 to 80 per cent.

7. In dilute solutions the blood is pink and presents a characteristic spectrum.

8. Late symptoms and after effects: These are quite lasting in man. They may be due in part to impurities in the gas. The late symptoms are prolonged unconsciousness or mental dullness, headache, nausea, a spastic condition of the limbs, and epileptiform seizures. There may be loss of memory and mental derangement for months. Pneumonia may follow.[1]

Kühne transfused defibrinated blood in amount not greater than one fifth the total blood mass of the animal, and no more than this amount was ever removed by bleeding. His conclusions are as follows:

1. Animals which are poisoned to a degree at which there is complete insensitiveness of the conjunctiva, recover without artificial aid in case their respirations have not fallen below 2 per minute.

2. Animals whose respirations have been reduced to 1

---

[1] The above statements have been largely based on Sollman's Pharmacology and Haldane's article in Hale White's Pharmacology.

per minute by carbon monoxid poisoning do not recover without artificial aid. For such animals a medium blood withdrawal is soon sufficient to restore sensitiveness of the conjunctiva, regularity of the respiration, and a rapid, moderately regular heart action.

3. If the respirations are abolished, even for only a few minutes, through the poisoning, no return to life can be obtained by means of artificial respiration and withdrawal of blood, in spite of the heart continuing to beat.

4. After a minute-long cessation of the respirations (seven minutes was the maximum time observed), and up to the time when no arterial pulse or heart beat was perceptible (the latter as felt through the chest wall), the animal being fallen into a state of unconsciousness preceded by a severe chill or by tetanic stretching of the entire body, transfusion of fresh oxygen-laden blood brought back life. The respirations began at first to return in a scarcely perceptible manner, but increased after about ten minutes up to 16 per minute, while the pulse soon became regular and rose at the same time to from 100 to 120 per minute. Thereupon the animal apparently quickly awakened, usually uttering loud cries, and after some hours there was nothing more striking to be observed than slight tremors. Finally, the transfusion removed any apparent traces of the poisoning.

There is this criticism to be offered concerning Kühne's experiments. He groups his cases largely on a basis of the rate of respiration. The author has found that this is very irregular, so much so that one could never definitely say that the respiration was 2 or 1 a minute. In fact it is difficult to say when respiration has finally stopped. A large majority of the dogs stopped breathing for two or even five minutes, and then began again with a fairly good quality of respiration. Therefore many of Kühne's good results may have been due

to the fact that he began his measures during this first interval of cessation of respiration, and his dogs were not so near death as he thought.

This research was undertaken to test the value of various therapeutic measures suggested, especially blood transfusion. Dogs were used. Ether was the anesthetic. Various forms of apparatus were used. The last one was a large, air-tight iron tube into which ordinary coal gas from the street main and air entered through water bottles, the bubbling enabling the observers roughly to gauge the amount. No attempt was made to determine the exact proportion of gas in the mixture. It was decided, owing to the varying susceptibility of the animals, that the best basis for comparison of therapeutic measures would not be the percentage of gas, its quantity, or its time of action (that is, within narrow limits), but rather the exact condition of the animal as determined according to ordinary clinical means, and especially by a manometric tracing of the blood-pressure. Consequently, the carotid artery was attached to a manometer with a style writing on a revolving drum in the usual way. A tracheal cannula was inserted and connected to a T-tube. The two branches of the T-tube were connected to valves made of fingers of rubber gloves set in small flasks. One valve opened with inspiration, the other with expiration. The valves were connected respectively with the gas tank and the outside air, so that the dog inspired the gas mixture and expired into the outside air. The dogs were thus poisoned, and when the blood-pressure reached a certain low point the various therapeutic measures were instituted and their results compared.

In all cases respiration had stopped. In the 16 cases recorded on the drum the heart had stopped in 8 before any measures of resuscitation were taken. As soon as the heart stopped, however, these measures had to be begun. Resusci-

tation was never accomplished after the heart had stopped for a few minutes. In 6 cases the heart had almost stopped, with a blood-pressure varying from 8 to 20 mm. of mercury, an average of a little under 14 mm.; certainly a low blood-pressure. In 2 cases the blood-pressure was 54 and 44 mm. One was saved by transfusion, the other died, notwithstanding the giving of saline infusion. Further details follow:

(*a*) Animals treated by bleeding, rhythmic pressure on the thorax, and artificial respiration. One experiment; 1 death.

(*b*) Animals treated by bleeding, intravenous saline infusion, rhythmic pressure on the thorax, and artificial respiration. Three experiments; 3 deaths.

(*c*) Animals simply treated by rhythmic pressure on the thorax and artificial respiration. Two experiments; 2 deaths.

(*d*) Animals treated by blood transfusion, bleeding, rhythmic pressure on the thorax, and artificial respiration. Ten experiments; 7 recoveries; 3 deaths.

When reduced to a low degree of blood-pressure, 7 out of 10 were rescued by transfusion of blood; 6 other dogs treated by the various other methods all died.

Of cases in which the heart stopped:

1. Transfusion saved 3 out of 6.
2. Intravenous saline infusion. No recoveries; 1 death.
3. Simple manipulation. No recoveries; 2 deaths.

Of cases in which the heart almost stopped:

1. Transfusion saved 4; 1 died.
2. Intravenous saline. No recoveries; 2 deaths.

These experiments include only those done while taking a blood-pressure record on the manometer, so that the exact condition of the dog could be constantly watched.

A large number of experiments have been discarded in which no drum record was taken, because it was found that

if the exact status of the dog were judged clinically—that is, by pulse rate, respiration, etc.—the results were so variable and so far from following any rule that one was forced to the conclusion that the point for beginning the various therapeutic measures was not the same, hence the conclusions could not be exact enough to be of value. Instead of an experiment with exact limitations cases were being produced such as are treated in the hospitals.

By recoveries are meant cases in which the blood-pressure came back approximately to the point where it started and remained fairly constant for an hour or so, and in which the respirations became spontaneous and of good quality again, and the reflexes reappeared. Actual recovery experiments were not done because of the difficulty of maintaining asepsis while taking blood-pressure records with a cannula in the carotid artery.

Conclusions.—1. Transfusion seemed to be of greater therapeutic value than the other measures employed in treating illuminating gas poisoning in dogs.

2. For an animal to recover it was necessary to begin transfusing immediately after the heart finally stopped beating.

CHAPTER XII

TRANSFUSION FOR TRANSPLANTABLE LYMPHOSARCOMATA IN DOGS

This research was undertaken with the collaboration of Dr. S. P. Beebe. The laboratory work was done in the Loomis Laboratory of Cornell University Medical College, under the auspices of the Huntington Fund for Cancer Research of the General Memorial Hospital.

No phase of experimental cancer research has aroused more interest than the demonstration of an immunity subsequent to the spontaneous recovery from implanted tumors. The truth of this principle has been established by numerous observations in several laboratories during the last three years, and yet there are a few observations in the older literature on the spontaneous retrogression of experimentally inoculated tumors. Wehr in 1883 noted the spontaneous retrogression of tumors developed by transplanting fragments of a medullary carcinoma in dogs. Smith and Washbourn in 1897 noted the spontaneous retrogression of tumors developed by planting fragments of a round-celled sarcoma found on the sexual organs of dogs, and they made the further very noteworthy observation that after spontaneous healing of the tumors there existed an immunity which protected against further implantation. Leo Loeb in 1902 noted retrogression of many of his transplantable sarcomata in rats. Sticker in 1904 confirmed Smith and Washbourn's observations on the spontaneous retrogression of the sarcomata in dogs.

It is, however, only within the last three years since the transplantation of carcinoma and sarcoma in mice and rats, that the importance of this retrogression in the tumor process has been appreciated. The authentic demonstration that these transplantable mouse carcinomata retrogress spontaneously in a varying percentage of cases and that subsequently there exists an immunity sufficient to protect the animal against further inoculation of like virulence, is one of the fruits of American cancer research, and although this work of Gaylord and Clowes was at first rejected by some investigators, notably Bashford and Ehrlich, it is now accepted everywhere as one of the foundation principles in cancer investigation. These results, with the additional demonstration by the same investigators that the serum of the spontaneously recovered animals contains some substances capable of inhibiting the growth of the tumor, have led directly to the present experiments.

The possibilities of a serum therapy for malignant tumors have been the subject of experimental investigation in many laboratories, and we have strong hopes that some procedure which will be in accord with the method by which nature inhibits the process and finally absorbs the tumor mass may be applied therapeutically. In this relation the most important facts regarding immunity which have been determined by the experimental work of the last five years are the following:

First.—A certain percentage of animals are naturally immune to tumor implantation.

Second.—A certain percentage of those animals which can be successfully implanted recover spontaneously and the tumors are completely absorbed. (The percentage of these two groups depends largely upon the virulence of the tumor.)

Third.—The spontaneously recovered animal may not be successfully implanted a second time with tumors of like virulence.

Fourth.[1]—There is no known method of rendering a susceptible animal immune except by the actual growth and subsequent retrogression of the tumor.

The nature of the immunity possessed by the spontaneously recovered animal or by the naturally immune animal is at present a subject for active discussion. It does not seem to correspond exactly to the immunity developed toward infections, and yet the serum of the recovered animals seems to exert a harmful action on living tumor cells. It has been repeatedly observed that any influence such as unfavorable hygienic surroundings, unsuitable food, repeated hemorrhages which diminish the general resistance, also decrease the immune forces opposing the tumor growth.

Ehrlich's idea that tumor growth is a matter of suitable foodstuff or, if not of foodstuff directly, then some intermediate group which permits the tumor cells to make use of the circulating foodstuff already present, is an ingenious attempt to explain the process, but it fails to account for the many varied facts already discovered. A further discussion of the relation of his theory to the present work will be given in the following pages.

The demonstration by Gaylord and Clowes that the serum of the immune animal had an injurious effect on tumor cells and that in some instances it seemed to aid in the inhibition of a growth already implanted, led us to try the effect of the direct transfusion of the whole blood of a spontaneously recovered (and therefore immune) animal to an animal with actively growing tumors. The method was that described elsewhere in these pages, so that details need not be repeated here. We aimed at transferring as much blood as possible; the mu-

---

[1] During the past year several reports have appeared dealing with immunity. It is probable that various methods may suffice to immunize an animal against tumor implantation such as inoculations with organ- and embryonic-tissue extracts.

cous membrane, the conjunctiva, even the skin in each case became red. In a few instances urticaria was noted on the abdomen.

The experiments forming the basis of this report were made on a series of dogs affected with a transplantable lymphosarcoma. Such a tumor has been the subject of observation and experimental transplantation by a number of investigators, the first publication, that of Novinsky, appearing in 1887. Wehr in 1883, Duploy and Cazin in 1894, Geissler in 1895, Smith and Washbourn in 1897, Powell White in 1892, Sanfelice in 1904, Sticker in 1904, Bashford, Murray, and Cramer in 1905, and Beebe and Ewing in 1906, have described tumors found upon the genital organs of dogs. In most instances there have been observations on the transmission of these tumors by coitus, but the histological diagnosis of the different observers has not been identical. However, as one reads the description of the process, one is more and more convinced that these men have all been dealing with the same type of growth, and that it is similar to the tumors which have been under observation in this laboratory during the last two years.

There is a difference of opinion among the various investigators who have studied the growth as to whether or not it is a real tumor. Wehr and Geissler call it carcinoma, Novinsky, Smith and Washbourn, Sanfelice, Sticker, Beebe, and Ewing agree that the tumor is sarcoma, while Powell White calls it a contagious growth; and Bashford, Murray, and Cramer are positive that the facts can only be explained by calling it an infectious granuloma. The controversy, therefore, is between those who believe the process is an infectious granuloma and those who believe it to be a true tumor. The dispute may not be settled by the histological examination, for Bashford, Murray, and Cramer agree that the histological appearance, the local mode of origin, its mode of growth from

its own elements, the impossibility of transferring it to other species of animals are tumor attributes. The chief arguments by which they dispute the tumor nature of the growths are the following:

First.—The infectious character of the process, as evidenced by its mode of transmission—i. e., by coitus.

Second.—Necrosis of tumor grafts and development of the new tumor from the surrounding connective tissue cells of the host.

Third.—Identity of the transplantation experiments with the processes which arise after injection of tubercle bacilli.

Fourth.—The more frequent occurrence of the tumors in young adult dogs and their comparative infrequency in older animals.

It is our purpose to examine critically these arguments and state our position with reference to them. With regard to the mode of transmission, it is a matter of common observation that coitus in the dog is a peculiar act, and one that is in most cases accompanied by some abrasions of mucous membrane. If in addition either animal has an ulcerating tumor on the genital organs, the possibilities are very great of infecting the other by transplantation of tumor cell to abraded surface. In the laboratory we have repeatedly shown that it is only necessary to rub a freshly cut tumor over a raw surface in order to secure a subsequent growth. It is worth while to note besides that this tumor has in the course of nature been subjected to repeated transplantation in such manner, and as we know from the recent laboratory work the transplantation of a tumor through a series of susceptible hosts raises its virulence, so we should expect this tumor to be more readily transferred than others which have not had such a history. The mode of transmission of the tumor is the result of a somewhat unusual combination of factors which

are not incompatible with the acceptance of the growth as a neoplasm.

The second argument is of much greater significance than the first. If it is true that a graft of the tumor when implanted in a new host suffers a complete necrosis while a new process grows from the surrounding connective-tissue cells of the host, then we are surely dealing with an infection and not a tumor. On this point we have the experimental evidence of Beebe and Ewing as follows: when a graft of a freshly cut tumor is implanted subcutaneously in a new host the larger part of the graft necroses, but there remains a layer of living cells about the periphery of the piece sharply separated in many places from the tissue of the host, and it is from these cells that the new tumor develops. These experiments have been made a number of times, and there is no doubt of the interpretation of the findings. Moreover, Bashford, Murray, and Cramer admit that in more rapidly growing tumors the chief part of the growth arises from the tumor cells, and the transformation of the fibroblasts is not always in evidence. When the small wound made by transplanting the graft becomes infected, the whole series of events is obscured and the relations of the cells of the host in the formation of the tumor may be very uncertain. When metastases of the tumor are found in the liver, lung, and kidney the cells are sharply separated from the tissues, and in no case can we find any evidence of a gradual metamorphosis of host cell to tumor cell. The behavior of tumor grafts when transplanted affords the most conclusive evidence regarding the nature of the suspected tumor, and in accepting the results of Beebe and Ewing, which are in direct contradiction to those of Bashford, Murray, and Cramer, we find that this method of experimentation demonstrates the tumor character of the process.

The third argument in opposition is answered by the ex-

periments of Beebe and Ewing just quoted. There is in these transplantation experiments no evidence of a similarity between the processes reactive to tumor transplantation and to injection of tubercle bacilli.

As regards the fourth argument, the tumors are not found exclusively upon young animals. Many older animals show the tumor, and in most instances it pursues a more malignant course in the older animals. The method of transmission favors its occurrence in larger numbers in young, adult, sexually active animals, and it is a well-recognized clinical observation that sarcoma is more commonly found in young individuals and carcinoma in those of advanced age.

A critical examination of the objections of Bashford, Murray, and Cramer reveals, therefore, nothing which is not compatible with the tumor idea, and which is not best explained and understood by considering the growth a neoplasm. There is in addition a considerable amount of collateral evidence which points in the same direction, viz., the tumor produces general metastases which lead to a fatal issue; no method of infection in which anything less than a living cell has been transferred from one host to another has ever given tumor growth. The range of temperature to which one may subject the tissue and still have growth, indicates that the critical points are those of a highly developed protoplasm and not of a microörganism. No microörganisms have been found which bear any relation to etiology, although Ewing has studied a large number of the artificially transplanted as well as primary tumors. In a few instances spiral organisms have been found on the ulcerated surfaces of some of the tumors, but in no case in nonulcerated tumors. Even in the ulcerated growths the spiral forms are found only a short distance from the surface, and it is now well known that such organisms are abundant on most infected ulcerating surfaces, and their pres-

ence has no etiological relation whatever to the process under discussion. From the total available evidence, we are convinced that the growth is a true tumor.

In the following pages we give the actual details of each transfusion. By comparing these with the diagrams of the tumors we believe an accurate idea may be gained of the course of events in each experiment. Following these experimental records, we propose to discuss their significance in regard to tumor immunity. The tumor animals had in every case been kept under close observation for some weeks prior to the transfusion, and only those whose tumors had never shown any tendency toward spontaneous regression were chosen as recipients for the transfusion.

PROTOCOLS OF EXPERIMENTS

EXPERIMENT 1

Recipient.—Dog No. 133. Long-haired mongrel; weight, 17 kilos. Planted December 6th in the same lot with Dog 125. Four tumors developed and grew slowly at first, but more rapidly later, and at the time of the transfusion they were in a flourishing condition.

Donor.—Dog No. 289. A strong, healthy animal, weighing 19 kilos, and in excellent physical condition. He had been planted previously in a group of six dogs that gave 55 per cent growth, but he failed to take the tumor. This donor was, therefore, naturally immune.

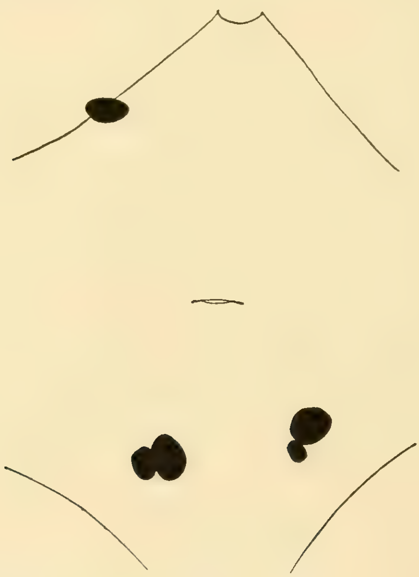
Transfusion.—March 20th, Dog No. 133 bled 600 c.c. and transfused with 1,500 c.c. from Dog 289. In five days following the transfusion the tumors of Dog 133 began to regress, and the absorption continued steadily (see Fig. 35) until the tumors had been entirely absorbed. The animal was replanted with the tumor on June 11th, and again on August 28th, without growth.

EXPERIMENT 2

Recipient.—Dog No. 125. Medium-sized, curly-haired mongrel; weight, about 14 kilos. Planted on December 6th by trocar; four

A.—Tumors on date of transfusion,
March 20, 1907.

B.—April 8, 1907.



C.—April 27, 1907.

Fig. 35. Experiment i.—Transfusion for Lymphosarcomata in a Dog.
After April 27th the tumors disappeared completely.

abdominal tumors developed by January 17th, and continued to grow rapidly. On February 23d tumor No. 3 was partially removed and plants were made from it into the back of the same animal.

Donor.—Dog No. 163. Short-haired mongrel; weight, about 16 kilos; had grown tumors six months before. They had completely regressed, except a small nodule on the abdomen, which remained stationary for some weeks. To determine whether the animal was yet immune he was planted on December 14th. No tumors developed, but the old nodule increased in size for two weeks, and then completely regressed. The animal had no tumors on March 20th.

Transfusion.—March 20th, 500 c.c. of blood were withdrawn from the femoral artery of the recipient, and the same quantity put into his femoral vein from the donor, No. 163.

Regressive changes were seen in the tumors of Dog 125 on March 25th, and by following the charts it will be seen that this regression continued steadily until the tumors on the abdomen had been completely absorbed, the time required being about eight weeks.

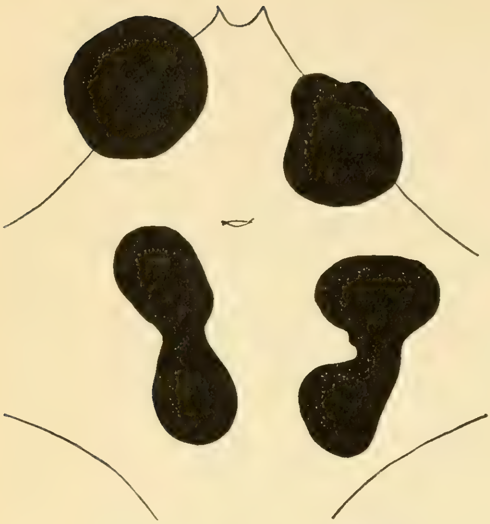
On April 20th a metastasis appeared in the right groin (see Fig. 36), and on April 12th, May 1st, and May 16th the tumors previously planted on the back began to grow. Because of this growth it was determined to do a second transfusion, using as a donor Dog 133—the animal cured by the previous transfusion.

Transfusion No. 2.—May 21st, Dog No. 125 was bled from the jugular vein, but through an error the amount of blood was not measured. 550 c.c. of blood were transfused from Dog 133.

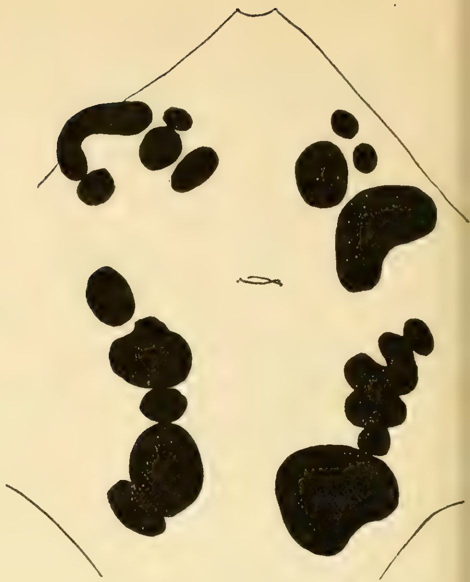
Following the transfusion the tumors regressed for a time, and then became stationary. Later they began to grow very slowly, so that it was determined to do a third transfusion.

Transfusion No. 3.—The donor, Dog 278, had been cured by a previous transfusion (see Experiment No. 4 a). August 29th, Dog 125 was bled 600 c.c. and transfused with 300 c.c. We intended to make a much larger transfusion, and were disappointed in the amount actually transferred. The tumors continued to grow very slowly. A fourth transfusion was determined.

Transfusion No. 4.—The donor was Dog 491, an animal of about 13 kilos weight that had previously grown tumors, but had spontaneously absorbed them. Dog 125 was bled 600 c.c. and transfused with 550 c.c. from Dog 491. Five days later Dog 125 had a secondary hemorrhage at the seat of operation, and was so weakened by it that he died.



A.—Tumors on date of transfusion, March 20, 1907.



B.—Second transfusion because of growth on the back, April 18, 1907.

C.—May 18, 1907.

D.—July 6, 1907.

FIG. 36. EXPERIMENT 2.—TRANSFUSION FOR LYMPHOSARCOMATA IN A DOG.

EXPERIMENT 3

Recipient.—Dog No. 116. Black and tan; weight not recorded. This animal was in very poor physical condition at the time of this transfusion. Tumors were planted on January 7th. The first growth of tumors was noticed on February 13th. Mange developed in the animal about January 30th, and the disease, together with the increasing growth of the tumors, had made the animal very cachectic.

Donor.—Dog No. 244. Fox terrier; weight not recorded. This animal was not in good physical condition at the time of the transfusion. He had grown four small tumors previously, and they had completely regressed. Following the transfusion, Dog 244 was again planted with the tumor, with positive results in each plant, and metastases formed in a few weeks. Therefore the immunity which he possessed at the time of the transfusion must have been very weak. Dog 244 will be referred to in a later transfusion.

Transfusion.—March 20th, Dog No. 116 was bled 400 c.c., and received 600 c.c. from Dog 244. The tumors of Dog 116 were not affected by the transfusion; they continued to grow steadily, and the animal died on April 17th in a very cachectic condition.

EXPERIMENT 4a

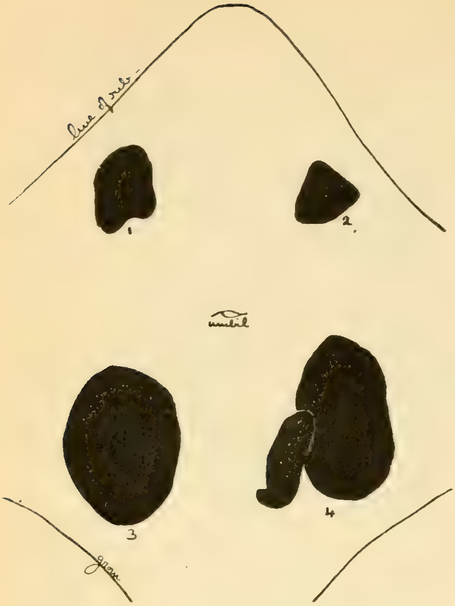
Recipient.—Dog No. 278. Mongrel; weight, 15.5 kilos. Planted on February 2d. Two tumors appeared on March 7th, and the remaining two on March 28th. At the time of the transfusion he had four good tumors, which had been growing rapidly.

Donor.—Large, vigorous animal, which had never grown the tumors, was used as a donor. He had been received at the laboratory on the day previous to the transfusion.

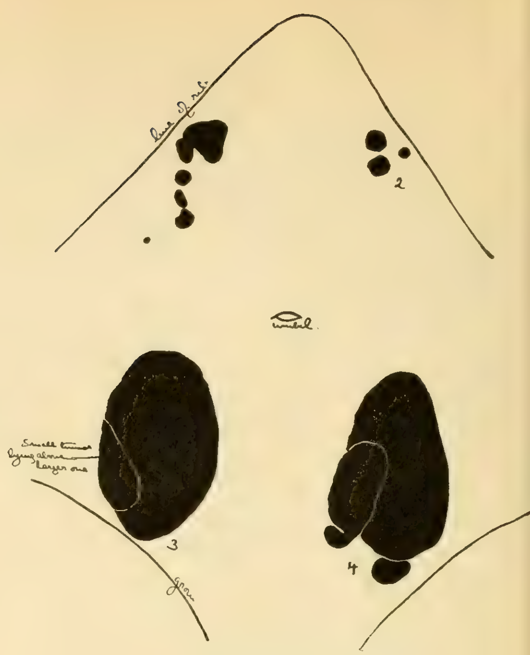
Transfusion.—May 21st, Dog 278 was bled 430 c.c., and received 1,500 c.c. from this donor. Following the transfusion his tumors rapidly regressed (see Fig. 37). All the tumor tissue was absorbed by July 20th. The animal was replanted on August 2d, and again on August 28th, but there was no growth from these grafts.

EXPERIMENT 4b

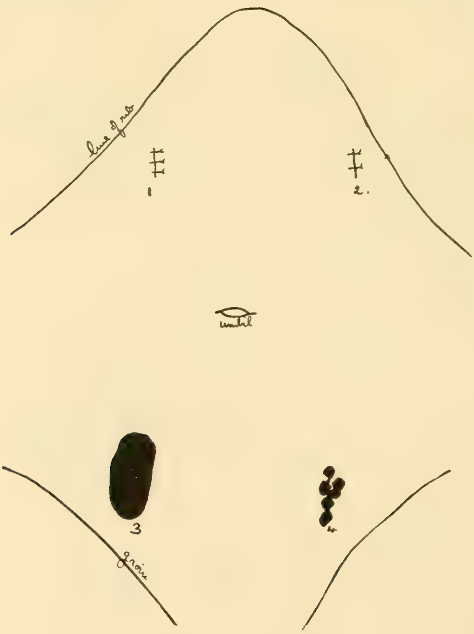
Donor.—As a part of the same experiment, the blood from Dog 278, the recipient in the previous transfusion, was passed into Dog 115.



A.—Tumors on date of transfusion, April 22, 1907.



B.—May 24, 1907.



C.—June 25, 1907. Two very small tumors were removed on this date for histological study.

FIG. 37. EXPERIMENT 4, a.—TRANSFUSION FOR LYMPHOSARCOMATA IN A DOG. By July 20, 1907, the tumors had disappeared completely.

Recipient.—Dog No. 115 was planted on January 7th, with negative results. The animal was then bled from the carotid in order to reduce his resistance, and following the hemorrhage he was again planted with tumors on February 14th. The plants all gave positive growth, but after reaching the size of a hickory nut they began to regress.

Transfusion.—The transfusion was done in this case to determine whether the blood from a dog (No. 278) growing tumors rapidly would stop the regression if transfused into an animal with regressing tumors (Dog 115). Dog 115 was bled 230 c.c. and transfused with 430 c.c. from Dog 278. The tumors of Dog 115 continued to regress, though at a slower rate than before the transfusion.

EXPERIMENT 5

Recipient.—Dog No. 132. Short-haired mongrel of 15 kilos weight. Planted on March 10th. Tumors developed April 6th, and continued to grow well until the day of the transfusion.

Donor.—Dog No. 275. Planted on February 4th. One small tumor developed, but it had been completely reabsorbed before the transfusion.

Transfusion.—May 21st, Dog 132 bled 300 c.c., and transfused with 500 c.c. from Dog 275. Following the transfusion the tumors in Dog 132 began to regress, and the absorption continued steadily until the tumors were entirely gone. The animal was planted on June 11th, and again on August 28th, without any growth resulting.

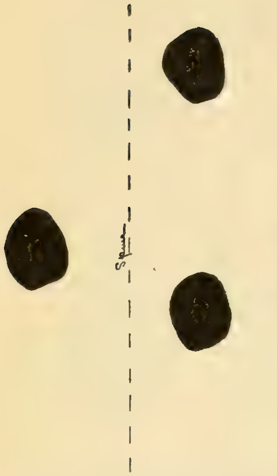
EXPERIMENT 6

In this experiment the same animal was transfused three times on different occasions.

Recipient.—Dog 137. Short-haired mongrel; weight, 7 kilos. Planted on March 2d. Tumors first appeared on April 6th, and continued to grow steadily (see Fig. 38).

Donor No. 1.—Dog No. 157. Mongrel; weight, 9.5 kilos. This animal had been planted in the same group with Dog 137, but failed to grow the tumors, and was, therefore, supposed to be naturally immune.

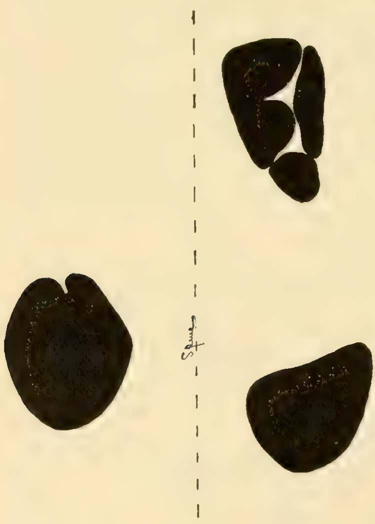
Donor No. 2.—Dog No. 282. White bulldog; weight, 10 kilos. Had been planted on January 30th, and again April 1st, with negative results in each case, and was, therefore, supposed to be naturally immune.



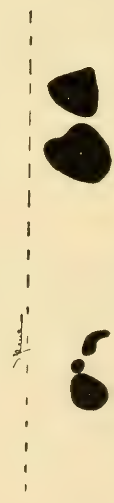
A.—Tumors on date of first transfusion, May 3, 1907.

B.—Tumors on date of second transfusion, May 21, 1907.

C.—Tumors on date of third transfusion, June 10, 1907.



D.—July 2, 1907.



E.—July 27, 1907. The small tumor on the left had been removed for histological study.

FIG. 38. EXPERIMENT 6.—TRANSFUSION FOR LYMPHOSARCOMATA IN A DOG. By September 24, 1907, the tumors had disappeared completely.

Donor No. 3.—Dog No. 274. Setter of 17 kilos weight. The animal was planted on February 4th, with positive results, four tumors developing and growing to a considerable size, but later retrogressing, and only very small fragments were left of the tumors at the time of transfusion.

Transfusion.—No. 1.—May 3d, Dog 137 was bled 140 c.c., and received 450 c.c. from Dog 157. As a result of the transfusion the tumors of Dog 137 became somewhat softer, but continued to grow (see Chart, p. 266).

No. 2.—Since May 3d, Dog 137 had lost 0.5 kilo in weight, and was in poorer physical condition generally. May 21st, Dog 137 was bled 225 c.c., and received 425 c.c. from Dog 282. The tumors continued to grow.

No. 3.—On June 10th, Dog 137 weighed 1.5 kilos more than on the date of the last transfusion, May 21st. The general condition had not improved with this increase in weight, and the tumors had continued to grow. It seemed best to do a much larger transfusion. On the date given, June 10th, Dog 137 was bled 500 c.c. and given 750 c.c. from Dog 274. Following this transfusion Dog 137 improved very markedly in physical condition and the tumors began to regress. On September 24th the last fragment of tumor had been absorbed. This animal was replanted with tumors August 28th, but no growth resulted.

EXPERIMENT 7

Recipient.—Dog No. 199; weight, 9 kilos. Planted on November 3d, with negative results. Planted a second time on December 14th. Growth of plants first apparent on January 17th. On March 23d, April 1st, and April 12th small pieces were removed to serve as seed for additional plants in other animals. On May 3d, the date of the first transfusion, Dog 199 had four tumors, which had been growing rapidly during the three weeks immediately preceding. The animal was in fair condition.

Donor.—Dog No. 273. Mongrel setter; weight, 12 kilos. Planted on February 4th. Growth on March 7th, continued until April 10th; at the time of the transfusion two nodules about the size of a grain of wheat remained to be absorbed. Dog in good condition.

Transfusion.—May 3d, Dog 199 was bled 150 c.c., and transfused with 550 c.c. of blood from Dog 273. Following the transfusion Dog 199 improved in general condition and gained 1 kilo in weight during the following two weeks, but the tumors began to grow.

Donor No. 2.—Dog No. 271; weight, 13.5 kilos. Was planted February 4th, with negative results, and again on April 1st, with the result that two small tumors developed. They grew to the size of a hazel nut, but were completely reabsorbed on May 13th. Dog in fine condition.

Transfusion No. 2.—May 21st, Dog 199 was bled 220 c.c., and immediately transfused with 700 c.c. of blood from Dog 271. Following the transfusion the tumors did not grow larger, but they did not begin to regress markedly until three weeks later, at which time it was evident that they were being absorbed. Regression continued steadily until the tumors had been completely absorbed, September 19th. Replanted on November 2d, without growth. (See Fig. 39.)

EXPERIMENT 8

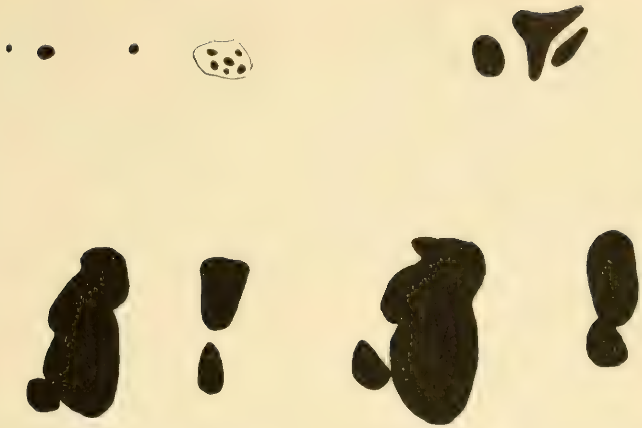
Recipient.—Dog No. 244. Fox terrier; weight not recorded. This animal has been referred to in Experiment No. 3. Following his use as a donor in that experiment, he was replanted with the tumor, March 23d. Three of the four plants gave growth on or before May 13th, and the general condition of the animal became progressively worse. When the tumors had reached the size of hickory nuts they were treated with various bacterial toxins by Dr. Tracy, but the results in this case were negative, and it was therefore determined to resort to transfusion.

Donor No. 1.—Dog No. 123; weight not recorded. Was planted with tumors on December 14th. Visible growth appeared on January 10th, and continued well until January 30th, on which date toxin treatment was begun by Dr. Tracy. The treatment resulted in a complete cure of the tumors. On May 4th, and again on July 11th, the animal was replanted with tumor grafts, but no growth followed in either case, and our conclusion was that the animal must possess some degree of immunity.

Donor No. 2.—Dog No. 132, an animal previously cured by transfusion (see Experiment 5).

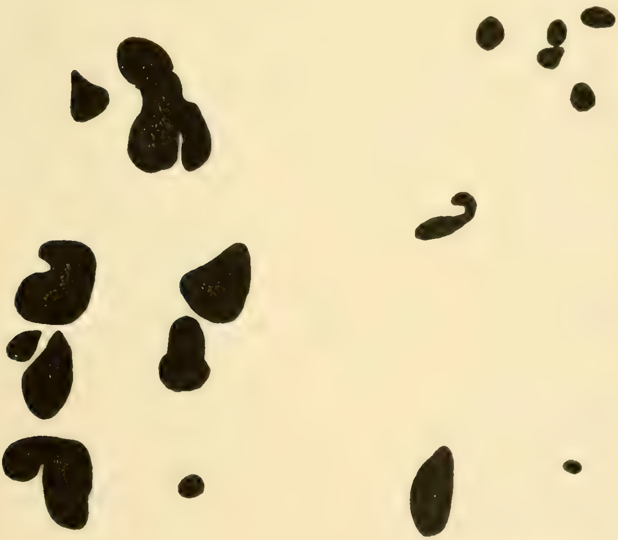
Transfusion No. 1.—July 31st, Dog 244 was bled 325 c.c., and immediately transfused with 550 c.c. of blood from Dog 123. The transfusion did not have much effect on the tumors, however, as they continued to grow, and the animal grew worse in general physical condition.

Transfusion No. 2.—August 26th. At the time of the second transfusion Dog 244 was very cachectic. He was bled 225 c.c., and transfused from Dog 132. Unfortunately, through the mistake of



A.—Tumors on date of first transfusion, May 3, 1907.

B.—Tumors on date of second transfusion, May 24, 1907.



C.—July 1, 1907.

D.—August 8, 1907.

FIG. 39. EXPERIMENT 7.—TRANSFUSION FOR LYMPHOSARCOMATA IN A DOG. By September 19, 1907, the tumors had disappeared completely.

an assistant, Dog 132 was not weighed immediately before the transfusion, so that we do not know exactly how much blood was taken from the donor. It was a satisfactory transfusion, however.

In spite of a marked hemolysis following the transfusion, Dog 244 gained in weight, his general physical condition improved somewhat, and the tumors soon began to regress. Although the tumors continued to regress (see Fig. 40), his general physical condition did not remain good. He gradually grew cachectic, and died on October 14th. At the autopsy it was found that the axillary, retroperitoneal, and mesenteric lymph nodes were enlarged. One of the retroperitoneal glands contained metastatic tumor growth, while the others failed to show it.

EXPERIMENT 9

Recipient.—Dog No. 444. Mongrel pointer; weight, 7 kilos. Planted on June 11th; tumor growth apparent on July 12th, and the growth continued steadily until the date of transfusion.

Donor.—Dog No. 435. Weight, 9 kilos. Planted on April 20th, with positive results, three out of four plants showing positive growth, but they never grew to large size, and soon began to regress. The process was complete on August 8th, and on the date of transfusion the animal was in excellent condition.

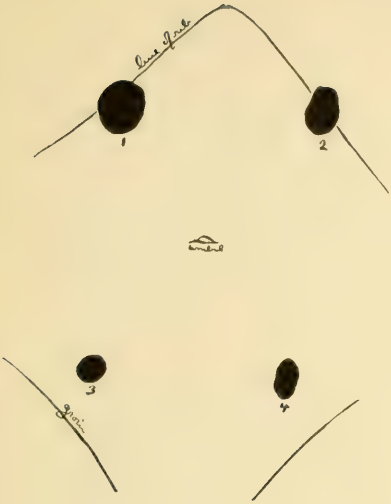
Transfusion.—August 27th, Dog 444 was bled 335 c.c., and received 450 c.c. of blood from Dog 435. The tumors showed evidences of regression in a few days after the operation, and the process continued steadily, our chart showing complete absorption on September 30th. The animal was replanted November 9th, and again on September 4th, without resulting growth.

EXPERIMENT 10

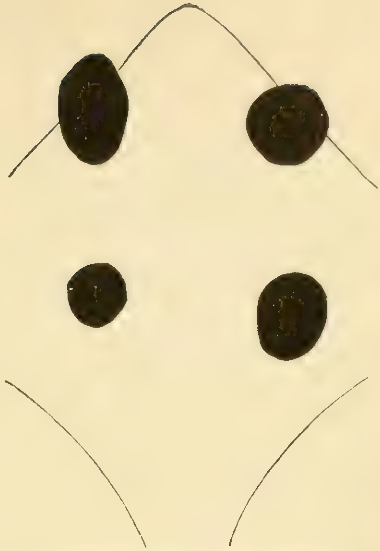
Recipient.—Dog No. 406. Mongrel setter; weight, 14 kilos. Planted March 23d. Growth visible on April 18th, and by May 20th four tumors had developed, and were growing well.

Donor No. 1.—The same animal which was used in the fourth experiment (a). He had lost 3 kilos in weight during the three weeks since his previous operation, and was in much poorer physical condition.

Donor No. 2.—Dog No. 269. A large, healthy animal, weighing 20 kilos. Tumors had been planted in this animal January 18th; the first growth appeared February 6th, and continued very slowly



A.—Size of tumors on June 3, 1907.



B.—Tumors on date of first transfusion, July 31, 1907.

C.—Tumors on date of second transfusion, August 26, 1907.

D.—October 9, 1907.

FIG. 40. EXPERIMENT 8.—TRANSFUSION FOR LYMPHOSARCOMATA IN A DOG. Although the tumors grew smaller the dog's general condition was poor. Death occurred on October 14, 1907. At the autopsy metastases were found.

until April 12th. Regression began at the latter date, and continued very slowly to a complete absorption.

Transfusion No. 1.—June 10th, Dog 406 was bled 550 c.c., and transfused with 1,250 c.c. from Donor No. 1. The tumors did not regress as a result of this transfusion, nor did the general condition improve.

Transfusion No. 2.—July 15th, Dog 406 was bled 700 c.c., and received 800 c.c. from the donor, Dog 269. Following this transfusion the tumors began to regress immediately, and the general condition of the dog improved. The absorption of the tumors was complete on August 17th.

GENERAL SUMMARY OF EXPERIMENTAL FINDINGS

From the table (page 266) we see that of the 10 animals which were treated by this method of transfusion, 7 were completely cured, in 2 of the remaining there was very marked effect from the transfusion, and only 1 died without showing any regression as a result of the exchange of blood. In this latter case there is more than a reasonable doubt regarding the immune condition of the donor, since the implantation of tumor grafts following the transfusion resulted in positive growth and subsequent development of large tumors.

Having determined the fact that a large transfusion of blood from an immune animal to an animal with growing tumors is followed by their regression and complete absorption, the questions at once arise:

1. By what mechanism is the result accomplished?

2. What is the value of different sorts of blood in this reaction?

3. What conditions of transfusion are best suited to give a favorable outcome?

We must say frankly that we do not know how the blood has caused the results noted. It is possible to maintain vari-

ous arguments on this point, but it is our purpose to put the facts on record rather than to theorize on the various possibilities in tumor immunity. We shall call attention to a few obvious relations which our work has to that of other investigators. Those who believe in atreptic immunity as outlined by Ehrlich will be inclined to argue that by the exchange of blood we have deprived the tumor of its specific foodstuff, and so it has merely died of inanition. Such a conclusion implies that the blood has negative action only, and that immunity is established by the exhaustion of specific foodstuff. The objections to the acceptance of such a hypothesis will become apparent as we proceed.

The histological picture of the regressing tumors is nearly the same as that of tumors regressing spontaneously, but in a few cases active degenerations were found in tumors regressing after transfusion which have no analogy in the spontaneously regressing tumors that we have studied. There is practically no evidence that the blood acts directly as a lysin—certainly not as a lysin of a high degree of activity. The action is spread over so long a time that highly active agents are practically ruled out. Until we know more of the nature of immunity to tumors, we can only say that these experiments indicate that the blood of the immune dog contains some expression of this immunity of sufficient potency to influence the course of tumor growth exposed to its action; perhaps by stimulating the general nutritive processes, for we see improvement in general physical condition follows transfusion. We know, too, that the blood of the tumor animal is hemolytic and perhaps generally toxic, so that the removal of such an injurious circulating medium and its replacement by the blood of a vigorous animal may possibly stimulate the latent defense of the tumor subject.

On the basis of so few experiments, we cannot decide

positively the relative value of blood from normal animals as compared with that of spontaneously recovered animals. Our impression is that the blood from the recovered animal is somewhat better than the normal blood, but the quantity of the transfusion as well as its quality are of value in determining the outcome.

In this connection we call attention to Experiments 4 and 10. The same donor was used for the first transfusion in each case. At the time the transfusion in Experiment 4 was done, the animal was in a strong, healthy condition. The transfusion in this instance was followed by complete absorption of the recipient's tumors. The donor lost weight, and his general physical condition became progressively worse in the interval between Experiment 4 and Experiment 10. The operative procedure in Experiment 10 was successful in every way, a large volume of blood being transferred, but no effect was produced on the tumors. It seems probable that the loss of blood in the first transfusion, together with the generally unfavorable physical condition at the time of the second experiment, left him in a poorer condition as regards tumor immunity. The second transfusion of Experiment 10, although of smaller volume, came from a spontaneously recovered dog in good condition and was completely successful in causing an absorption of the tumors. If the favorable result is due to the negative action of removing specific foodstuff, it would seem that the first transfusion should have been successful, since it gave a more complete exchange of blood than the second. Evidently some difference in the quality of the two bloods was responsible for the regression in one case and not in the other. Further evidence of this fact is afforded by Experiment 8, in which both donors had been cured of tumors and could not be replanted. The first transfusion from an animal cured by toxins was entirely unsuccessful, while the second from a previous

transfusion recovery was followed by a nearly complete regression of the growths.

In Experiment 3 we found that a spontaneously recovered animal did not give a satisfactory blood for the tumors of the recipient continued to grow. In this case, however, we found that subsequent planting of the donor gave positive growth—a condition which was not found in the other spontaneously recovered animals of our experiments.

In Experiments 6 and 7 we have evidence that the quantity of the transfusion is of some importance. In Experiment 6 the first two transfusions from naturally immune donors produced no effect on the tumors, while the first from a spontaneously recovered animal gave a much more complete exchange of blood and caused an absorption of the growths. We have no method for measuring the relative degrees of immunity possessed by the three donors further than the fact that all three would not grow the tumor, and it may be that the favorable outcome in the final transfusion was due to its quantitative aspects. If we consider that the recipient's total blood supply was 12 per cent of his body weight he had 840 c.c. circulating blood. In the first two transfusions an average of 180 c.c. of blood were removed and 437 c.c. added, so that the final volume of blood was 1,097 c.c., of which 40 per cent came from the donor. Following the same method of calculation, we find that in Experiment 7 the first transfusion which was unsuccessful was only 37 per cent, while the successful transfusion was 45 per cent.

It appears, then, that immunity may have two factors—one a common factor possessed to some extent by any strong, healthy, vigorous animal, in some cases of sufficient activity to prevent successful inoculation with tumors, and a second specific factor which is developed by the growth and regression of tumors. What qualitative relation these two factors have to one

SUMMARY OF LYMPHOSARCOMATA TRANSFUSION EXPERIMENTS

No.	Donor's Immunity	Recipient		Transfusion		Result
		Weight	Condition of Tumors	Cu. Cm. Bled	Cu. Cm. Transfused	
1	Natural immunity.	17 kg.	Growing well.	600	1,500	Complete absorption of tumors.
2	1. Spontaneous recovery.	14 kg.	Growing rapidly	500	500	Complete absorption of the first set of plants.
	2. Transfused recovery.	14 kg.	Growing slowly. (Second set.)	......	550	Regression at first. Growth later.
	3. Transfused recovery.	14 kg.	Growing slowly. (Second set.)	600	300	Tumors continued to grow slowly.
	4. Spontaneous recovery.	14 kg.	Growing slowly. (Second set.)	600	550	Death from secondary hemorrhage five days later.
3	Supposed spontaneous recovery.	7.5 kg.	Growing rapidly	400	600	Negative. Tumors continued to grow. Dog died a month later.
4	A. Unknown.	15.5 kg.	Large, rapidly growing.	430	1,500	Complete absorption of tumors.
	B. None.	12 kg.	Regressing slowly.	230	430	Tumors continued to regress but more slowly.
5	Spontaneous recovery.	15 kg.	Growing well.	300	500	Complete absorption.
6	1. Naturally immune.	7 kg.	Growing steadily.	140	450	Tumors became somewhat softer, but then continued to grow.
	2. Naturally immune.	7 kg.	Growing steadily.	225	425	No effect.
	3. Spontaneous recovery.	7 kg.	Growing steadily.	500	750	Complete absorption.
7	1. Spontaneous recovery.	9 kg.	Growing rapidly	150	550	General condition improved. Tumors continued to grow.
	2. Spontaneous recovery.	9 kg.	Growing rapidly	220	700	Complete absorption.
8	1. Cured by toxins.	8 kg.	Tumors growing well.	325	550	No effect.
	2. Transfusion recovery.	8 kg.	Very cachectic.	225	......	Almost complete absorption.
9	Spontaneous recovery.	7 kg.	Steady growth.	335	450	Complete absorption.
10	1. Same dog as Exp. 4 A.	14 kg.	Steady growth.	550	1,250	No effect.
	2. Spontaneous recovery.	14 kg.	Steady growth.	700	800	Complete absorption.

another, we cannot say on the basis of our previous knowledge. Although immunity to tumors does not seem to be analogous to bacterial immunity, nevertheless these results indicate that it is to some extent a blood condition which may be transferred to another animal, rendering him passively immune.

In regard to the conditions of transfusion which favor the regression of the tumors, it is our opinion that the donor should be a strong, healthy animal, immune to the tumor, and that a large replacement of the recipient's blood should be made, giving him from 25 to 50 per cent more blood than is removed. Such a conclusion has its foundation in our experimental results, and is what might be theoretically expected.

CLINICAL STUDIES

CHAPTER XIII

A GENERAL REVIEW OF THE MORE MODERN THEORIES AND PRACTICE OF TRANSFUSION

THE methods of transfusing blood arrange themselves into three groups according as to whether the blood is (1) introduced into the blood-vessels, (2) the peritoneal cavity, or (3) under the skin of the recipient. Then, whichever method is used, the blood may be (1) taken from an animal of the same species as the recipient (similar blood), or (2) taken from an animal of another species (dissimilar blood). If blood is introduced into the vessels of the recipient it may be (1) done by the immediate method (i. e., directly from vessel to vessel) or by the (2) mediate method (i. e., through a force pump or other instrument intended to increase the pressure of the flow). If the latter it may be injected either whole or defibrinated, or have chemicals added to it to decrease its coagulability. With either the mediate or immediate method the simultaneous injection of normal saline solution may be carried on in order to increase the total amount of fluid.

The greatest success has come from the use of similar blood. The experience of many years has shown that it is much safer than dissimilar blood. In large quantities the latter has caused death in man and animals. In small quantities the symptoms produced vary according to the amount injected, and the difference in species of the animals. In

human beings severe rigors followed by high fever, occurring usually in the first twenty-four hours, were often observed by Hasse and all his followers. Renal disturbances were not infrequent—partial suppression of the urine and hematuria (Hasse, Sander, Thurn, Klingelhoefer, Brugelman). Aveling (quoted by Roussel) had a patient die in one hour after the injection of 9 ounces of lamb's blood. Ponfick found with dissimilar blood, whether defibrinated or not, that dogs and rabbits always died after the injection of a large quantity in from thirty-six to forty-eight hours. There was almost complete anuria, and the kidneys were found to be greatly swollen, with granular and blood casts in the straight and convoluted tubules.

Landois was the first to show that the serum of one animal may have the property of destroying the red corpuscles of another. Hayem warns particularly against the use of dissimilar blood, and says that in transfusing from an ox to a dog a grave morbid condition resulted which presented a striking resemblance to purpura hemorrhagica, and death occurred in a few hours. He says: "The effect of a foreign serum on the circulating blood is such that the latter immediately becomes finely clotted (grumeleux), and carrying the thousands of clots into the small vessels one sees innumerable hemorrhagic infarcts formed."

Many hundreds of experiments and clinical experiences have shown that similar blood in itself is not usually dangerous. If once safely introduced into the circulation of the recipient, it does not produce the serious symptoms caused by dissimilar blood, although, as the experiments of Ehrlich and Morgenroth on goats have shown, a hemolytic action may occur. If this action does occur, the large number of successfully performed transfusions show that it is usually not serious.

After the transfusion of similar blood the excess of red

cells in the blood of the recipient is maintained for a certain length of time, during which they are supposed to carry on their functions as if they were in the vessels of the animal from which they came. Hunter gives the following table to show the time of the return of the blood to normal:

Worm-Müller.	Experiments on dogs.	Average time 17 days.
Quincke.	" " "	" " 17 "
Hunter.	" " "	" " 29 "
Von Ott.	" " "	" " 21 "

Golgi and Raggi state that the increase of hemoglobin continues during several weeks and even after twenty-seven days, and also that this increase can be obtained in normal animals as well as in those weakened by bleeding.

Schultz, in experimenting on rabbits, found at first there was a moderate fall in the blood count, but repeated counts made over an interval of from two to four weeks pointed to a retention of from 63 to 73 per cent of the number of the corpuscles injected. In his experiments, from one third to one half the total blood mass was removed and then replaced with defibrinated blood from other rabbits.

In regard to the retention of blood, Hunter says that the length of time depends (1) on the amount of blood transfused, and (2) on the condition of the animal at the time of the transfusion. Any condition in which metabolism is diminished, as in starvation, tends to prolong the life of the red corpuscles. On the other hand, any condition in which metabolism is active tends to shorten their life. "The quantities of blood transfusable in man are so small that, under the most favorable conditions, the life duration of the red corpuscles is probably rarely longer than two or three days." This last statement, while made in reference to man, seems hardly consistent or probable when compared with the figures given by Hunter himself and others after experimenting on animals.

As with the infusion of normal saline solution, an amount of blood so small that it seems out of all proportion to the amount of blood lost by a person dying from hemorrhage may save life. As far back as 1818 Blundell noticed this fact in experimenting on dogs. Dieulafoy cites two such cases, in one of which there had been extreme loss of blood after twenty days of epistaxis occurring at frequent intervals supposed to be due to hemophilia. On the twentieth day 120 gms. of blood were transfused with "complete success." The result was permanent after all other methods employed had failed. While the amount of blood lost was not known accurately, it was very great, and much larger than the amount of blood transfused.

The question as to whether or not blood acts as food when transfused is of interest. Hunter concludes that as it is not immediately destroyed, its nutritive value is not as great as blood taken by mouth. "We find that the loss of weight in starvation is unaffected by the transfusion of blood in whatever quantities and however often repeated, and this is the case even although at death the blood may not only be increased in quantity but be actually richer in quality than in health. Thus in one of Tchiriew's experiments in which transfusion had been repeatedly made and in which the weight had steadily fallen from 6.928 to 4.583 kilos, the quantity of blood obtained from the body amounted to about 8.7 per cent of the body weight as compared with the 7 per cent usually obtainable in health; and this blood contained 27.11 per cent of solids with 4.21 gms. of nitrogen, as compared with the 21 per cent of solids containing about 3.2 gms. of nitrogen usually found in healthy blood. Similar results were obtained by Panum, by a method, however, not as free from objection as that of Tchiriew, on whose results, as on those of Foster, the greatest reliance can be placed."

The blood is primarily a carrier, and a given amount of transfused blood would contain a certain amount of nourishment and a certain amount of waste material. When mingled with the blood of the recipient it would add the former to the resources of the recipient to be taken up by the tissues while the waste material would be excreted. The blood corpuscles would perform their natural functions unless there should happen to be hemolytic action, as there sometimes is between similar bloods, and would suffer the same fate as the corpuscles of the recipient. The objection may be raised that transfused blood would not follow this course, but as the weight of evidence is in favor of its acting just as the animal's own blood acts, the objection does not hold. In short, as borne out theoretically and by experiment, transfused blood is of very little, if of any, value as a food for the recipient. Large quantities of blood plasma would be much more likely to nourish than equal quantities of whole blood, but it is doubtful if enough could be injected to produce measurable results.

In Hunter's experiments on dogs and rabbits the curves showing the effects of intraperitoneal transfusion indicate in 5 cases a marked increase in weight of the animal, which usually began between the fifteenth and twentieth day. Whether this was due to excess of reaction after the equally marked primary fall, or to the stimulating effect of the transfusion is not evident. A series of observations extending over a longer time would have shown whether the gain over the animal's original weight was a permanent one or not. If due to the transfusion it would indicate that the latter might be of great benefit in treating various conditions. It could not be ascribed to the blood having acted as nourishment.

Intravascular Transfusion.—Of the three general methods of performing transfusion the intravascular one is by far the most important, and the one which has almost always been

employed. After the transfused blood reaches the vessels of the recipient, however, the effect is the same, regardless of the method of introduction. As far as the general effects of intravascular transfusion are concerned, Jennings, in his monograph, published in 1883, gives the following: "By combining the tables given by Bellina, Asche, and Leisrink, we get a total of 243 cases in which transfusion was performed for acute or chronic anemia prior to the year 1873. Of these 243 cases, 143 (40.9 per cent) terminated in complete recovery; in 34 cases (14 per cent) the operation was followed by temporary benefit, but failed to save life; in 95 cases (39.1 per cent) no beneficial result whatever was achieved. Accordingly, transfusion failed in a little over a third of all these cases, while in nearly two thirds of the total number it was followed by improvement or recovery. If we examine more closely into the details of each failure we find that in a vast majority of them death cannot be assigned directly or indirectly to the operation, but was due to other causes.

"In 113 of the cases alluded to above, the operation was performed on account of hemorrhage during or immediately after delivery. Of these 113 cases 67 ended in complete recovery, 7 showed only a temporary improvement, while 39 terminated fatally without any sign of previous amendment. A positive result was thus achieved in 65.5 per cent, or two thirds of all the cases belonging to this category."

Morton found, excluding some doubtful cases, that "in 103 instances of transfusion for what might be called pure post-partum hemorrhage, over 56 per cent recovered; while in 41 cases of hemorrhage after wounds, operations, etc., over 58 per cent recovered under this treatment." Whether any of Jennings's cases are included in his statistics is not known.

Oré collected a large amount of material from different sources, including most of the cases which had been treated

up to the time when he published his book in 1876. The following figures are from his tables:

	No. of Cases	Cured	Improved	Unchanged	Dead
Animal blood..........	154	64	20	44	26
Human blood..........	381	185	15	5	178
	535	249	35	49	204

They doubtless include many of the cases given by Jennings. In some of them defibrinated blood was used, and the transfusions were performed to overcome postpartum and other hemorrhages, anemias, insanity, tuberculosis, etc. The figures are of value only as showing the final outcome under all conditions. Probably a small percentage only of the deaths were due to the actual performance of the transfusion, as sufficient distinction was not made between the immediate and the late results. As far as the latter are concerned, there were doubtless many cases given as recoveries, when ultimately death resulted from the disease treated. The period of time covered was from 1667 to 1876.

The Injection of Air into the Vascular System.—In intravascular transfusion one danger which experience has shown must be carefully guarded against is the introduction of air into the blood-vessels. The chief factors influencing the results produced by the injection of air into the blood-vessels are (1) the amount of air injected, (2) the speed with which it enters the vessels, (3) whether the injection is made into a vein or artery, and (4) the region in which the injection is made.

Small amounts of air have frequently been accidentally or purposely introduced into the circulation without harm resulting beyond possibly a temporary tumultuous cardiac action and labored respiration. In animals the amount necessary to

cause disturbance seems to depend on the size and species of the animal. Senn found that a dog weighing 30 pounds would usually recover after an injection of 30 c.c., while double that amount was usually fatal. He found that sheep endured a proportionately larger amount. A large amount invariably kills, and usually almost immediately after the injection or introduction through the uterine sinuses after labor or in the course of surgical operations, particularly of the head and neck. Oré cites several fatal cases in man due to the accidental introduction of air during transfusion.

If air is injected slowly it is much less likely to prove fatal, provided the amount is not large, than if injected rapidly. The regularity of the injection has an effect also, as a given amount injected slowly and steadily all at one time is much more likely to kill than the same amount injected at intervals.

Senn found that the effect of injecting into arteries was different from that produced by injecting into veins. In both the result varied with the amount of air, but in the latter an equal amount was less dangerous. With a fatal amount death was due to acute cerebral ischemia and secondary venous embolism, and there was intense collateral engorgement of the vessels of the brain and of the spinal cord. Senn, with other investigators, has also shown that in the region of the great vessels of the neck, and wherever the venous pulse can be detected, there is greater danger than in other parts of the body.

Most observers agree that death from venous air embolism is caused by acute dilation of the right ventricle, as the right ventricle is always found to be in diastole at autopsy. Besides this Senn believes that there is acute cerebral ischemia and asphyxiation due to embolism of the pulmonary artery. He found that the resistance of an animal depended in part on the ability of its right ventricle to withstand dilatation, and

that the air was forced over into the left side of the heart through the pulmonary capillaries if the amount were small. Oré experimented on dogs and concluded that the paralysis of the right ventricle, and not of the other parts of the heart, was due to acute dilation, but also to a specific action of air in producing on the muscle of the right ventricle what he called a sedative effect. He tried injecting different gases—oxygen, nitrogen, and carbon dioxid—but did not find that they produced this last effect, and they could be injected in much larger quantities than air without fatal result.

In regard to treatment, Senn recommends puncture and aspiration of the right ventricle, and, if accessible through the accident having occurred through the jugular vein, catheterization and aspiration of the right auricle. He bases his recommendations on his experiments on animals.

On the other hand, Oré, with more regard for the exigencies which may arise in transfusion, recommends stimulation of the pneumogastric nerve by electricity in case of air embolism. In the presence of Longet and the members of the Commission de la Société de Chirurgie he killed one dog by injecting 90 c.c. of air into a vein at one stroke of the syringe. Into a second similar dog he injected 140 c.c. of air in the same way with symptoms of approaching death appearing at once. On placing one electrode from an electric battery on the dog's chest and the other on his neck and causing the current to flow, recovery resulted.

Intraperitoneal Transfusion.—In intraperitoneal transfusion there can be no doubt that blood injected into the abdominal cavity of an animal passes into the circulation (Orth, Tillmans, Hindenlang, Müller, Bareggi, Penzoldt, Wintrich, Cordua, Hunter, Obalinski, Maas, Grenet, Hayem, Golgi and Raggi, Corona and Loco-Pisani, Howe, and others). Doubtless there have been exceptions to this statement, but either

whole or defibrinated blood is usually absorbed in toto. Ledderhose stated that small clots are formed with all the blood eventually clotting, but he observed this only in fluid removed from the abdominal cavity after injection, where it would seem there might have been a chance for outside influences to have acted. In an experiment on a dog Howe found the peritoneum covered with a thin reddish film eighteen hours after injection of part of the dog's own blood, but as he does not state that it was clotted the finding is of no more significance than that for some unknown reason absorption was delayed. In another case he reports that there was a thick reddish coat present, but here again absorption was delayed, and it is no proof that the blood would not have eventually been absorbed. Wintrich found that blood in large quantities always coagulated sooner or later inside of twenty-four hours, but that small quantities were always absorbed.

As regards the increase in the number of red corpuscles in the blood of the recipient, Golgi and Raggi demonstrated that twenty minutes after an injection a progressive increase began. Southgate states that the maximum increase of corpuscular elements occurs inside of three hours. Hunter sometimes found a gain of from 20 to 30 per cent in from twenty-four to forty-eight hours, and with the animal actually losing weight. Obalinski detected an increase in as short a time as one hour. Maas found a gain of from 500,000 to 2,500,000 red corpuscles per cubic millimeter at the end of five hours.

With the increase of the red corpuscles there is naturally an increase of the hemoglobin also. Bizzozero and Golgi (quoted from Hunter) found an increase twenty minutes after injection. Foa and Pellacani (Hunter) found that intraperitoneal transfusion in dogs led to a hyperplasia and then to a true functional reddening of the bone marrow. Corona and Loco-Pisani state that the increase of hemoglobin begins after

twenty-four hours and continues for an indefinite time. Probably their observations did not extend over a long enough time to warrant the latter part of their statement. Golgi and Raggi state that the increase is a little less than the amount of the hemoglobin in the blood injected provided the injection is not too abundant.

The rate of absorption from the peritoneal cavity is variable. Wegner (quoted from Hunter) found that in some cases it was so great in the first hour that if it had been maintained at that rate the animal would have absorbed its own weight in twenty-four hours. Within certain limits a large amount was absorbed more quickly than a small amount. Thus in one experiment 134 c.c. out of 200 c.c were absorbed in one hour, while in another only 5 c.c. out of 100 c.c. were absorbed in the same time.

When blood enters the peritoneal cavity the peristaltic movements of the intestines doubtless act in conjunction with the force of gravity to diffuse it to a certain extent and thus facilitate its absorption. On the part of the peritoneum there is a temporary exudation of serum, and a transmigration of leucocytes into the peritoneal cavity with a resulting temporary increase in the number of red corpuscles in the animal's blood (Ledderhose, Hunter). This increase is probably followed by a short period of dilution as the exudate and the serum from the injected blood are absorbed, and then by a true increase in the number of red corpuscles as the red corpuscles are absorbed.

From experiments on animals Dubar and Remy found that there were two great paths of absorption—through all the lymphatics of the mesenteries, and particularly of the diaphragm and the blood path represented by the radicals of the portal vein. They found that grains of coloring matter were only absorbed through the diaphragmatic channels, and also that

absorption was most rapid at that point. Starling and Tubby found that coloring matters in solution were absorbed rapidly by the blood-vessels with an accompanying interchange between the blood and the fluid in the cavity, but they say nothing about the absorption of solid particles. Grenet states that the blood corpuscles are absorbed chiefly via the subdiaphragmatic and perineal lymphatics after the plasma has been absorbed. Southgate, Recklinghausen, Ludwig, and others found that the pleural surfaces of the diaphragm were injected and often distended with blood after absorption. Hayem believed that the lymphatics played an important part, but that it was impossible to say that they were the only means of entrance into the circulation. While the presence of stomata in the peritoneum is denied by Kolossow and Muscatello, it is now generally accepted, and the probability is that while the plasma passes through the cell walls by osmosis, and also through the stomata directly, the red corpuscles and most of the white corpuscles enter the lymphatics only through the stomata.

Following intraperitoneal transfusion there is usually a mild degree of inflammatory reaction which only lasts a short time. Hunter says that it always occurs, and Hayem found it absent only when similar blood was used. Ledderhose found it present when defibrinated blood from the same animal or from one of another species was used. Howe says that the mild reaction following the use of similar blood was likely to be replaced with peritonitis with dissimilar blood. According to Corona and Loco-Pisani, the peritoneum does not suffer. Landerer and Mosler both had fatal cases, their patients dying from peritonitis.

The length of time that transfused corpuscles remain in the blood of the recipient has already been considered in discussing intravascular transfusion.

As a whole, the intraperitoneal transfusion of blood is of

interest as a method only. Under proper aseptic precautions it should be done with safety, and while the benefit from it is not had as quickly as with other methods, there is no danger of causing embolism, which is a point in its advantage, as even if clotted blood should get into the abdominal cavity it would do no harm. However, the other methods have always been preferred, and are as a whole more desirable to follow.

Subcutaneous Transfusion.—The subcutaneous transfusion of blood was first proposed by Karst, of Kreusnach, who in 1872 injected defibrinated blood under the skin of a rabbit. Landenberger was the first to apply the method to man. He used defibrinated animal's blood. After Landenberger, Jullien, Malassez, Poncet, and Ponza were among those who interested themselves in this method, but it has never attracted as much attention as the other methods.

As in the case of intraperitoneal transfusion, the blood passes into the circulation of the animal into whose tissues the injection is made. It would be expected that the blood plasma would be absorbed, just as any other fluid injected subcutaneously is absorbed, and that the corpuscles suffer the same fate, at least in part, is proved as well. Bareggi (quoted by Ziemsson and Hunter) injected defibrinated blood subcutaneously, and found well-preserved corpuscles in the thoracic duct three hours afterwards. He also found them as late as three days after the injection, and was able to demonstrate their presence in the large lymphatics near the site of the injection. Worm-Müller (Hunter) produced extravasations in dogs by severing arteries subcutaneously. As early as twenty minutes afterwards he found red corpuscles in the neighboring lymph glands and lymphatics, and later in the thoracic duct. Ziemsson says: "There is not only an increase in the fluid quantity of the blood, but an actual transplantation of the blood cells."

As one of the strongest advocates of this method, Ziemsson

goes on to say: "But the most certain proof to me that the introduction of defibrinated human blood into the human circulation of itself causes no symptoms of hemoglobinuria and ferment intoxication is to be found in the complete freedom from reaction after subcutaneous blood injections, if these be made correctly. An injection of 200 to 350 c.c. of defibrinated blood, a quantity which is completely absorbed, causes neither fever of any consideration, nor dyspnea, nor hemoglobinuria; in short, there are no troubles except the local pain of the injection. . . . Intravenous transfusion may endanger life. . . . The case is very different when the subcutaneous cellular tissue is selected to receive the blood. Here every danger is excluded, as the connective tissue retains the blood clots and particles of air as a fine sieve, and by a proper method of injection no blood residuum is produced, or certainly does not lead to phlegmonous inflammation." Other advantages which he claims are the saving of time, the elimination of the danger of dilating the right heart, and the absence of the necessity of operating.

Ziemsson's method consisted in the employment of strict asepsis, the use of chloroform when the amount of blood to be transfused was large on account of the pain of the massage ("absolutely necessary") and the employment of defibrinated blood kept at from 37° to 40° C. As the site of an injection he selected preferably the outer and inner aspects of the thigh. The needle of a 25 c.c. syringe was thrust through the skin deep into the subcutaneous cellular tissue, and the blood slowly injected while an assistant rubbed "over the point of the injection with all his strength. This is an important point, as it is to prevent an abscess, but the massage must dissipate the blood at the very time it leaves the cannula." This was repeated in different places until the requisite amount was injected.

Ziemsson has seen but two cases of suppuration following many injections which he has made, and in both they were due to avoidable faults in technic. He says that the increase in hemoglobin in the patient's blood is greatest within the first twenty-four hours after the injection, and then it falls gradually during the next few days. As a rule, there remains an excess above the quantity present before the injection, though there were several cases of severe anemia from different causes in which the condition before the injection was reached again in a few days. After a longer or shorter time repeated injections may increase the hemoglobin gradually, though a primary increase and secondary decrease is repeated after each time.

Landenberger only noticed the formation of an abscess once at the point of injection " when in the haste an unsuitable blood was mixed with venous blood as its dark color showed." He also states that venous blood injected into the phthisical patients remained under the skin a long time, as shown by the persistence of the pain and swelling. He attributed this to the skin being " subparalytic."

On the whole, subcutaneous transfusion is of more interest historically than of value practically when compared with intravascular transfusion.

The transference of blood from one individual to another can be safely and efficiently done only by the union of the supplying vessel of the donor to the receiving vessel of the recipient in such manner that the continuity of the intima of each vessel is continuous with that of the other. This has not, so far as the author is aware, been hitherto accomplished.

CHAPTER XIV

THE DIRECT TRANSFUSION OF BLOOD

As has been shown by the brief historical account in the preceding pages, the greater part of transfusion as formerly performed was done crudely and empirically before the development of bio-chemistry, physiology, pathology, and bacteriology to a degree at all approaching the present stage of development. Good hospitals were unknown as we know them to-day. Many accidents arose from infection, passage of blood clots into the circulation of the recipients, and air embolism. Moreover, there was often an unfortunate selection of cases. It was natural, therefore, that the advent of saline infusion as a substitute for transfusion should have been hailed with enthusiasm, and that the latter should have been almost entirely superseded by it.

Almost as far back as we have historical records the idea of the replacement of lost blood with other blood has appealed to the imagination of mankind. From superficial consideration it would certainly seem to be an ideal treatment, and the persistent attempts to employ it in the face of the known dangers which surrounded its use show how strongly this view has held sway. The present research was begun in 1898, using the method of Mosso. This proved to be impracticable. The essential need of a safe method which would meet all the requirements not being fulfilled, it was necessary to wait until an opportunity such as that afforded by the work of Carrel appeared.

By following Carrel's technic it is possible to sew together the ends of two severed blood-vessels in such a way that when the blood is allowed to flow through, the joint does not permit leakage, the flow is uninterrupted, and clotting does not occur. This method may not only be used for temporary anastomosis, but for permanent restoration of function. As developed by the author in performing transfusion directly from one individual to another, the suture method was employed in all the early experimental and clinical work, but it was found that a special cannula and method of using it took less time. In the later work the cannula has come to supersede the suture for making all temporary anastomoses. Both methods, however, will be described in detail. In order to appreciate the possibilities presented by the classic work of Carrel and Guthrie, the reader should consult their many publications. Watts has recently published an admirable summary of the work of other investigators in surgery of the blood-vessels (*Bull. Johns Hopkins Hosp.*, 1907).

THE SUTURE METHOD OF BLOOD-VESSEL ANASTOMOSIS

Instruments and Materials.—From an experience with over 100 blood-vessel anastomoses made in the laboratory, and more than 60 clinical cases, the following instruments and materials have been found to be most helpful: (1) scalpel; (2) blunt dissector; (3) small, sharp-pointed straight scissors for dividing the vessels, snipping off fragments of the adventitia, etc.; (4) ordinary dissecting forceps; (5) minute tissue forceps with exact approximation at the points (those used by watchmakers have been found to be useful); (6) half a dozen mosquito hemostats to use in securing the minute branches of the radial artery and the small venous branches; (7) a pair of small "Crile" artery clamps; (8) No. 16 English needles

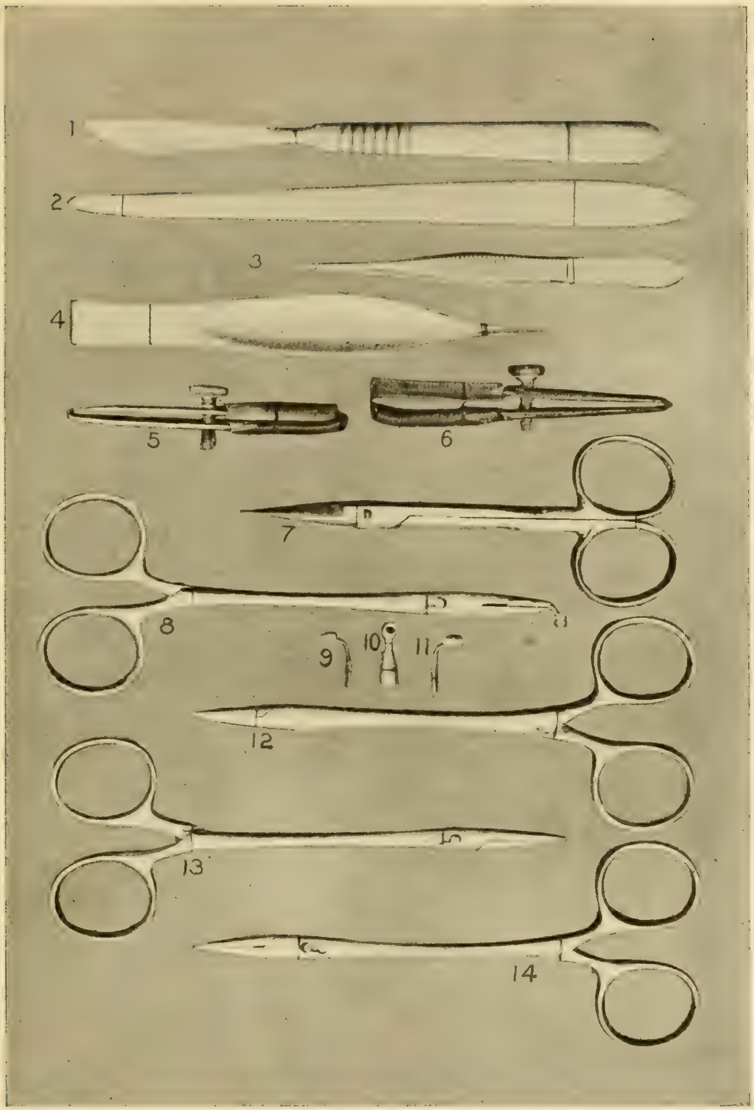


FIG. 41.—INSTRUMENTS USED IN PERFORMING A TRANSFUSION BY END-TO-END ANASTOMOSIS BY THE CANNULA METHOD. 1. Scalpel. 2. Blunt dissector. 3, 4. Fine-pointed forceps. 5, 6. "Crile" clamps for temporary closure of blood-vessels. 7. Fine-pointed scissors. 8. Hemostat with transfusion cannula locked in place. 9, 10, 11. Three of the set of four cannulæ. 12, 13, 14. Mosquito hemostats for placing the blood-vessels. (Reduced to about one half actual size.)

(Kirby's); (9) No. 1 Chinese twist silk; (10) sterilized vaselin; (11) the ordinary means of closing a wound, and dressings (see Fig. 41).

After experimenting with different kinds and sizes of needles it has been found that the No. 16 round needle as made by Kirby, of London, is the best. A No. 14 or 12 size is larger and easier to handle, but has the disadvantage of causing unnecessary traumatism of the intima and tends to permit oozing through the needle holes when under pressure. Any other than a round needle of about this size will be found to be unsatisfactory.

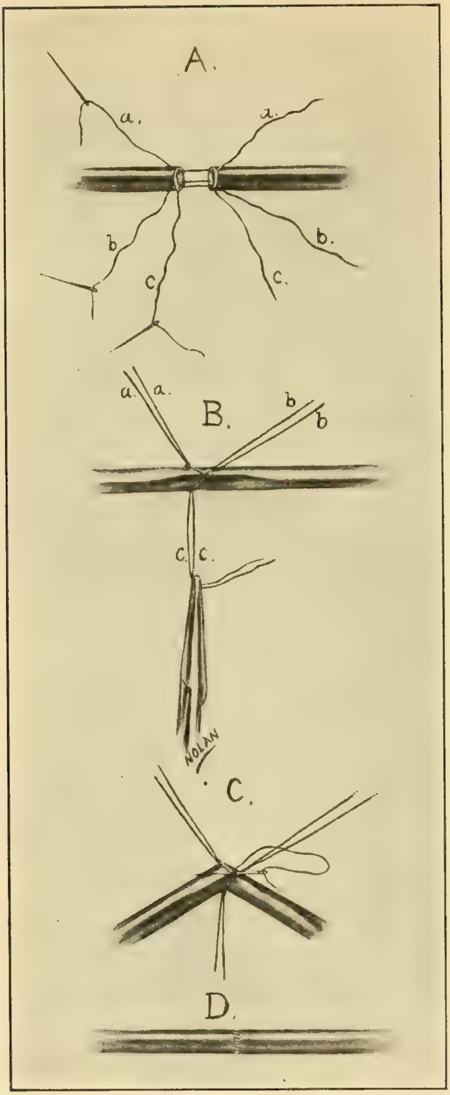
As a No. 16 needle is scarcely larger than a hair, the problem of threading it is a difficult one. The method finally adopted to secure suitable sutures was to take a piece of the No. 1 Chinese silk or "000 linen" about 2 feet in length, attach a hemostat to the lower end, carefully separate the upper end into its component strands for a long enough distance to permit each being grasped by the hands of the operator and a hand of an assistant, and then, allowing the hemostat to swing free and pull downward as the twist in the silk made it revolve, hold the silk until it was untwisted down to the hemostat. This gave strands capable of being threaded through the tiny eye of the needle, and with these strands the sewing was done.

In order to thread a needle, such a strand is gently pulled at the end in the direction of its long axis until the end breaks. This leaves tiny fibrils which may then be twisted together and passed through the eye. To preserve the threaded needle, it is passed in and out at 2-inch intervals through a long narrow strip of gauze, from which it can easily be withdrawn when needed. By placing several threaded needles in one strip they may all be sterilized together.

Operation.—Having the ends of the vessels to be united sufficiently near each other, the adventitia of the artery is

drawn down over the end by means of the fine-pointed dissecting forceps, and cut squarely off with the small straight scissors. By so doing the adventitia left on the vessel retracts and leaves a free field for inserting the sutures. The vein is likewise prepared. Then, with the fine silk strand thoroughly saturated with sterile vaselin or oil, the needle is passed through all the coats of the artery from without inward near the cut surface, and passed through the end of the vein wall in the opposite way. The two vessels are brought intimately in contact by tying the suture. The ends of the suture are not cut close to the knot, but about 4 inches from it. This gives a stay suture to hold while completing the technic. Two more similar stay sutures are inserted with the circumference of each vessel divided into thirds between them, and if the stays be drawn taut the closely approximated ends of the artery and vein are divided into 3 equal parts, so as to form an equilateral triangle (Carrel and Guthrie).

With the three stay sutures successfully placed the problem becomes a comparatively easy one. Tension is brought to bear on any two of the stays—it is immaterial which two as long as the third one lies underneath. On the third stay an inch below the vessels is attached a mosquito hemostat which is allowed to pull them down, and thus prevent the needle from being passed through the lower part of the vessel walls when the final sutures are placed. The weight of the hemostat is too small to damage the walls, but great enough to insure complete retraction of the lower angle. With the three stays thus held a continuous over-and-over suture is run between the upper two, placing the stitches as close together and as near the ends of the vessels as possible, except near the stays, where they are placed a little farther away in order to include the stay stitch holes. With one third completed, the tension is shifted to the next two stays, and the hemostat shifted to the



third stay, which is thus brought underneath. This is repeated once more, and by that time the anastomosis is completed and ready for the blood to flow through. It should be remembered that the venous clamp should always be removed before the arterial clamp. If this is not done the blood rushes against the venous clamp under arterial pressure, and throws too great strain on the anastomosis, and may cause leakage. Even if one or two drops of blood exude when the clamps are

Fig. 42.—Diagrams of Stages of End-to-End Anastomosis of Two Blood-vessels by the Suture Method (Carrel). *A*, Method of placing the three stay-sutures. They are equidistant and pass through the entire thickness of the vessel walls. *B*, The stay-sutures tied, and the lower angle retracted by the weight of a hemostat. *C*, Placing the over-and-over continuous suture between two of the stay-sutures. The vessels are lifted by the upper sutures in the hands of an assistant, so as to make an angle between the vessels. This permits easy sewing with the straight needle. *D*, The anastomosis completed.

properly removed no further leakage will follow, provided, of course, that the sutures have been properly placed. The operation is one of great delicacy, and it is essential that the vessels should be handled with extreme gentleness, and just as little as possible, to avoid running any risk of causing clotting (see Fig. 42).

THE CANNULA METHOD OF BLOOD-VESSEL ANASTOMOSIS

While Dr. S. J. Mixter, of Boston, was the first to call the author's attention to the possibility of this method, Queirolo, as far as has been ascertained, was the first to use an anastomosis tube in blood-vessel surgery as it is used at the present time. Even then the fundamental principle did not originate with him, but with another investigator, who used it in making intestinal anastomoses. Later Payr developed the idea much more extensively, and was the first to suggest using tubes made of magnesium (the metal) which would be absorbed in the tissues and permit the formation of permanent anastomoses. Neither Payr nor Queirolo employed the short handle attached to the tubes which permits easy control with hemostatic forceps until fixed in place—an essential improvement. Payr suggested holding them by means of clamp or other forceps with fine points which could be inserted into the lumen of the tube with the entering vessel, but it is obvious that this method would not be utilizable with very small vessels owing to lack of room in the tube.

Queirolo's description of his method is as follows: "The isolated portion of the portal vein is drawn through a short glass tube, pulled back over its forward edge, and bound firmly upon it. . . . The glass tube thus covered by the vein is now drawn into the free end of the vena cava, which is then bound

on the glass tube, so, however, that the first loop which fastens the portal vein is not covered by the vena cava. The artery compression forceps are loosened, and thereupon the blood streams out of the portal vein into the vena cava without touching a foreign body, and only coming in contact with the vessel endothelium, for the first loop touches only the outer wall of the portal vein, and the second loop only the outer wall of the vena cava. . . ." (Moleschott, *Untersuch.*, 1895, xv, 228–40).

The cannula such as the author now uses was developed in collaboration with Dr. F. W. Hitchings. To be able to use vessels of different sizes different-sized cannulæ have been made, the smallest with an inside diameter of 1.5 mm., the next half a millimeter larger, and so on up to 3 mm. It has been found by experience that this range covers all ordinary cases in the human subject.

The instruments used when the cannula is employed are the same as those used in carrying out the suture technic, except that the cannula replaces the No. 16 needle and fine suture. The vessels to be anastomosed are exposed in the same way (the details will be described under the heading of the general management of a transfusion in the following pages), and after selection of a cannula of size suitable to the size of the vessels the end of the vein is either pushed *through* the handle end of the cannula with the help of fine-pointed forceps, or pulled *through* by means of a single fine suture inserted in its edge, the needle being left on the suture and passed through the cannula ahead of the vein. The handle of the cannula is then tightly seized by a pair of hemostats (the fingers are too clumsy), 3 mosquito hemostats, or small, self-locking forceps such as oculists use, are snapped at equidistant points on the end of the vein, taking care not to have the tips extend up into the lumen more than is necessary to get a firm hold. The end of the vein is then cuffed back over the cannula by gentle

simultaneous traction on the 3 hemostats, and tied firmly in place with a fine linen thread in the groove *nearest to the handle.* The cuffed part is next covered with sterile vaselin, being careful not to get any into the open end. This facilitates slipping the artery over the cuff. The hemostats are removed from the vessel edge, and the artery may then be put in place.

Owing to the elasticity of the arterial wall it usually shrinks considerably when the pressure from within is removed, as it is at the free end. To obviate this it may be necessary to dilate the end *very gently* by inserting the closed jaws of a mosquito hemostat covered with vaselin, and opening them for a short distance. The 3 hemostats are then applied to the edges just as with the vein, and the artery is gently drawn over the cuffed vein on the cannula and tied in place with another fine linen suture applied in the remaining groove. The mosquito hemostats are removed, and finally the large hemostat which has been snapped on the handle of the cannula during all this time is removed. The process is then completed. After the transfusion the cannula is removed, both artery and vein are ligated, and the wounds are sutured (see Fig. 43).

In making a cannula anastomosis experience will show what size cannula is suitable for the given vessels. As large a size should be used as possible without injuring the intima of the artery by stretching it too much. Usually there will be no difficulty in obtaining a large vein, but the artery may be very small. If too small a cannula is used, the amount of the flow will be diminished. Moreover, too large a vein will take up too much room in the cannula, and the amount of flow be diminished.

The author has never yet found a radial artery so small that the 3 mosquito hemostats could not be applied to its edge

to draw it over the cuffed vein. If preferred, 3 stay sutures may be used instead of the hemostats, but they will tear out much more easily, and are not so easily or so quickly applied.

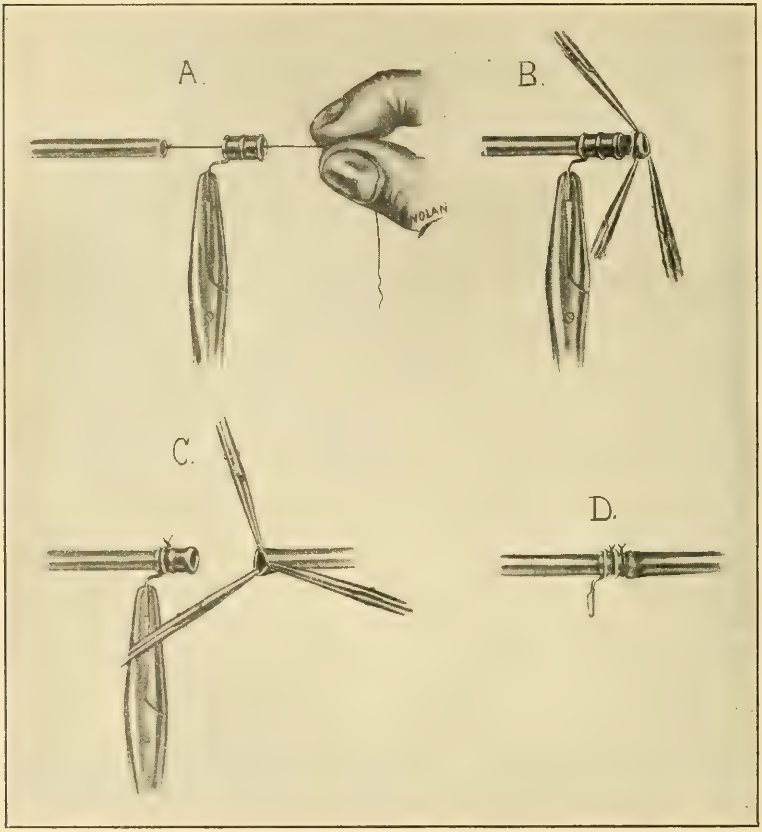


FIG. 43.—DIAGRAMS OF STAGES OF END-TO-END ANASTOMOSIS OF TWO BLOOD-VESSELS BY THE CANNULA METHOD (as modified by Crile and Hitchings). *A*, Pulling the vein through the cannula. Very fine pointed forceps may be substituted for the single suture. *B*, Cuffing back the vein over the cannula with three mosquito hemostats. *C*, The vein cuffed and tied in place in the groove next to the handle of the cannula. The artery is ready to be drawn over the vein. *D*, The anastomosis completed, and the cannula hemostat removed. The artery is tied in the remaining groove. The short handle of the cannula is so light in weight that it does not cause torsion of the vessels.

In the earlier cases the artery was cuffed back instead of the vein, and the vein pulled over. It was found that cuffing back the artery in man obstructed the lumen of the cannula too much, and was often a very difficult procedure, especially when the wall was at all calcified. Besides, with a calcified wall there was too much danger of tearing the intima in the process of cuffing. Apparently there is no danger of clotting when done either way, but to cuff back the vein is the better method.

In using the cannula two facts should be particularly remembered. The first is that the long axis of the tube should coincide with the long axis of the lumen of the vein and artery. A little experimenting will show how easily the cannula may be made to slant so that the opening in it will come almost in contact with the artery wall, and shut off the flow in great part or completely. Actual experience has shown the necessity of placing the cannula accurately.

The second and less obvious fact is that unless the right amount of tension is maintained on the vessel which passes through the cannula when the blood is flowing across, particularly with a small cannula, the flow will be diminished or shut off altogether by the elasticity of the vessel wall on tension in the cannula pulling the outside part of the vessel in and blocking the way. This is more likely to happen with the artery drawn through the tube than with the vein, owing to the greater elasticity of the arterial wall. It may be very prettily demonstrated by drawing an artery through a small cannula, cuffing it back, and tying it in place. On removing the clamp controlling the flow no blood will appear at the open end of the artery, or at most the flow will be very small and weak. On putting gentle tension on the tube by drawing it out a little in the direction of the long axis of the artery, the wall puckered up in the cannula will

be pulled out and the blood will spurt sometimes as far as 3 feet.

The exposed vessels should be kept moist with warm normal saline solution. Not only is drying harmful, but the flow is increased through gradual relaxation of the arterial wall.

Experience has shown that if anything goes wrong in carrying out this technic it is best to start again from the beginning, and not to try to get around any of the details by substitution. For example, if one of the 3 mosquito hemostats slips from the end of the vessel which is being either cuffed or drawn over, the attempt should not be continued until the vessel has been removed and the hemostat is accurately replaced. Not only will valuable time be lost in trying to substitute ordinary forceps for the slipped hemostat, but the danger of tearing the intima is much greater. For the average surgeon, at least, it is essential to have the instruments lock firmly in place on the vessel edge. Then, if one be dropped from the hand it does not have to be reapplied when picked up. For this reason ordinary forceps are entirely unsuitable, and anyone endeavoring to use them takes on himself the responsibility of the possible occurrence of clotting, or of inability to finish the technic. Every detail has been worked out over and over again, and while there is doubtless plenty of room for improvement, it is felt that every detail should be exactly followed, at least until the operator has convinced himself that any modification is suitable. It will be found that the use of the anastomosis cannula is much less difficult than the use of the suture method, the results are more certain, and the time of operation much shorter.

THE GENERAL MANAGEMENT OF A TRANSFUSION

Having carefully considered the technic of end-to-end anastomosis of blood-vessels by the suture and cannula methods, we come to its practical application in performing direct transfusion from one human being to another. First of all a suitable donor must be obtained. It is assumed here that all the requirements have been successfully met, and that both donor and recipient are in readiness.

It is of great advantage to have a thoroughly trained corps of assistants. A full staff would include first and second assistants, a nurse to handle the sponges, sutures, etc., a nurse to devote herself entirely to the comfort of the patients, an instrument nurse to pass between the operating and sterilizing rooms, and an orderly. If special investigations are to be made—for example, of changes in the blood—others must be added as needed. All should be able to work noiselessly and rapidly.

The operating room should have all the ordinary equipment. Two operating tables are necessary, one for each patient. They should be of the type which allows the patient to be easily changed from a horizontal to a head-up or head-down position, so as to permit combating either cerebral anemia or acute cardiac dilatation. They should be well provided with pillows with which to make the patient as comfortable as possible. Two small square tables of the same height as the operating tables are also needed—one for the instruments, and the other to support the arms of the patients. Two low stools, one for the surgeon and one for the first assistant, complete the list.

From twenty to thirty minutes before being brought to the operating room the donor and recipient each receive $\frac{1}{4}$ of a grain of morphin hypodermically, unless there is some special

reason for its being contraindicated. The patients are assured that they will experience no pain beyond the first needle prick.

When each is in place on his respective operating table the tables are arranged so that the left arm of each will rest comfortably on the small square table placed for the purpose between the operating tables (see diagram, Fig. 44). In order

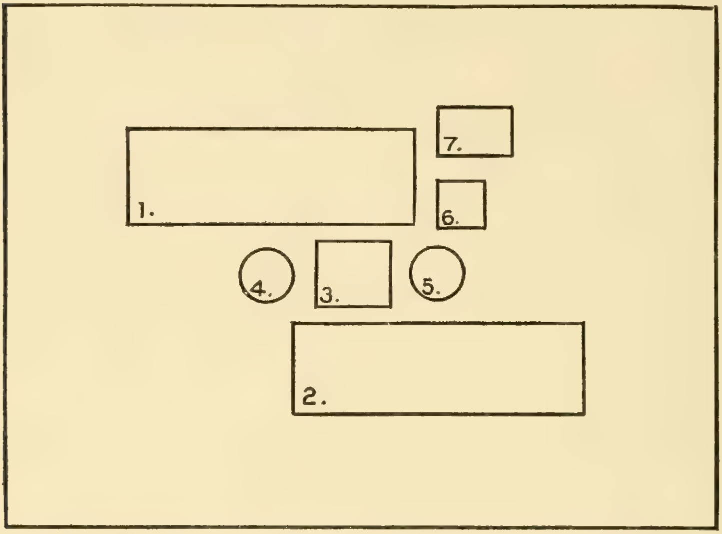


FIG. 44.—DIAGRAM OF ARRANGEMENT OF OPERATING ROOM FOR A TRANSFUSION. 1, 2. Operating tables for recipient and donor, respectively. 3. Table for arms of recipient and donor. 4, 5. Stools for surgeon and first assistant, respectively. 6. Instrument table. 7. Table for dressings, sutures, etc.

that no glimpses of the surrounding room may be had the face of each is covered with a damp towel "to avoid too much bright light and headache." The operator and first assistant sit between the operating tables on opposite sides of the small square table. The other small square table with the instruments on it is placed conveniently for the second assistant. The patients are again told that there will be no pain beyond the first prick. The nurse detailed to care directly for the

patients relieves the monotony of waiting by changing the wet towels, bathing the forehead, giving water to drink if desired, and in short doing anything permissible to afford comfort.

The next step is the dissection of the blood-vessels to be used. Experience has shown that it is best to use a radial artery of the donor and any superficial arm vein of the recipient near the elbow. Usually the median basilic vein is the best one on account of its size and easily accessible position.

Local anesthesia is obtained by injecting cocain in $\frac{1}{10}$ of 1 per cent solution with a few drops of 1-1,000 adrenalin chlorid solution. Several hypodermic syringes should be ready so that there need be no delay on account of having to stop to refill a single one. The injections are first made into the skin, and then more deeply around the vessels. After this, firm pressure is applied by the hand over a gauze sponge to insure thorough spreading of the cocain through the tissues. When carefully performed there is absolutely no pain in any part of the technic until the sutures are placed in the skin at the end of the transfusion. By then the effect of the cocain has usually worn away.

In making the dissection it is necessary to have good light. Mosquito hemostats are used to catch every vessel that sheds even a drop of blood. The field should be kept absolutely clear. The donor's radial artery is isolated for a distance of about 3 cm. at the point of election in the wrist. Here there are a number of small side branches which must be carefully isolated and tied with No. 1 Chinese twist silk (which has not been split up into strands) before being cut. The artery is then tied at its *distal* end, and a "Crile" clamp is gently screwed in place over the proximal part as near to the place where it comes out of the undissected tissues as convenient. The clamp should be screwed up with great care. Just enough pressure should be used to control the flow of blood without causing injury

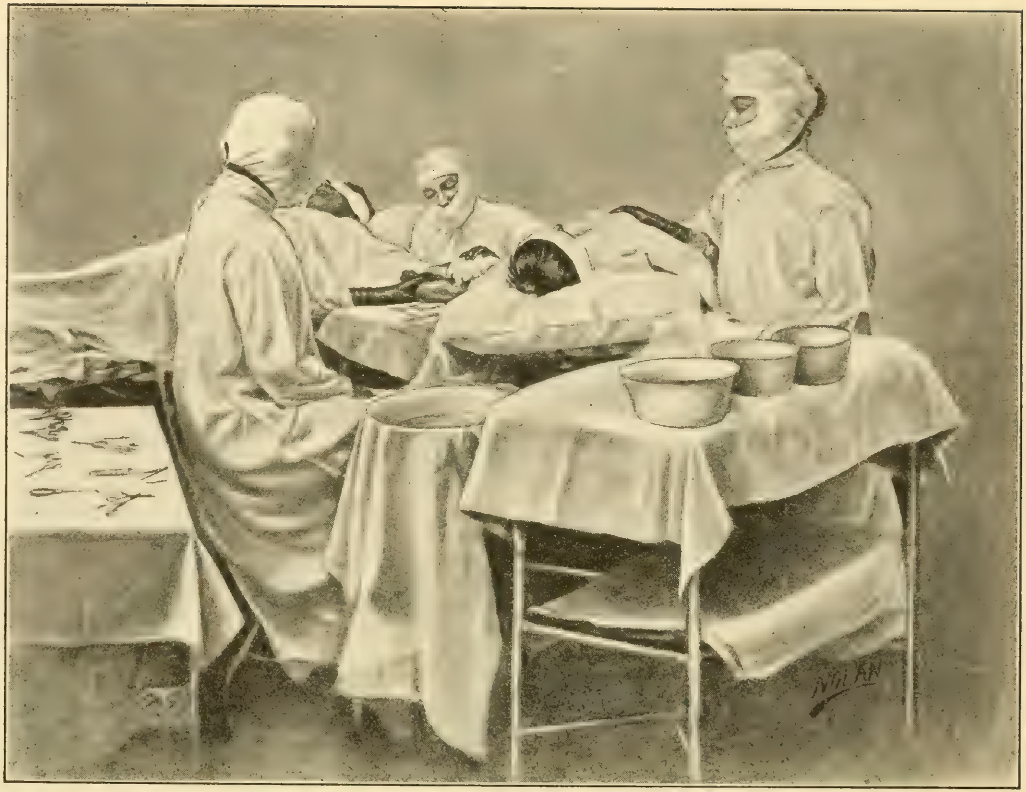


FIG. 45.—A CLINICAL TRANSFUSION IN PROGRESS. The donor is on the right, the recipient on the left. The actual connection between the artery of the donor and vein of the recipient is hidden between the arms.

to the vessel wall. The artery is severed with sharp scissors a short distance from where it is tied off, the end cut squarely across, the adventitia pulled down and cut off as directed under the technic of making an anastomosis by either the suture or the cannula method, and is then ready for the completion of the anastomosis. The result should be that the operator has about $2\frac{1}{2}$ cm. of exposed radial artery free from branches, the cut end open, and the blood prevented from coming out of it by the clamp.

The next step is the dissection of the vein. It is exposed for the same distance as the artery, the branches are tied off in the same way, and the ligature is also applied at the *distal* end. The second "Crile" clamp is applied just as before, the vein cut near the ligature, and it in turn is ready for the completion of the anastomosis.

The anastomosis is made either by the suture or the cannula method as described in the previous pages. The details will not be repeated here. It may be said that in practically all cases the cannula method should be used rather than the suture method. In order to meet possible emergencies, however, the operator should be prepared to carry out either. It seems to the author that neither should be attempted on the human subject until experience has been gained in the laboratory.

With the anastomosis completed, the questions which then arise are how much blood should be allowed to pass over, how fast to allow it to pass over, and what will happen if the limits of safety are passed. So many points must be considered in answering these and other questions that the problems presented by the donors and recipients will be discussed separately.

CHAPTER XV

PROBLEMS PRESENTED BY THE DONOR AND BY THE RECIPIENT

THE DONOR

It has been proved many thousands of times, either directly through hemorrhage or indirectly through transfusion, that loss of blood to even a considerable amount may occur and the individual survive. In normal individuals lost blood is quickly replaced.

Another fundamental fact is that while the blood of the donor may convey life to the sick person, it may also convey death in the form of disease. As far as can be determined the giver of the blood should be free from any constitutional or other disease which might be engrafted on the patient.

A donor may usually be readily obtained. Both men and women are suitable. In cases in which no immediate hurry exists the best subject is selected from among the relatives and friends who are willing to serve. The gravity of the patient's condition and the reason for wishing to transfuse are carefully explained in detail, and the painlessness of the operation to both donor and recipient is assured. Almost always the offer to serve is made voluntarily. In fact an entire family and numerous friends have frequently been eager to do so.

The only difficulty which has been encountered thus far has been among ignorant people, who may have a certain amount of distrust of both surgeons and hospitals. Even among such people, however, but one refusal has been experi-

enced. In this particular case the parents of the patient, a nine-year-old child whose legs had been crushed, refused to assist, their argument being that the child was so much mutilated by the injury that it was not worth saving!

In two instances among the author's cases donors were hired. In these instances the commercial attitude was apparent, and they were not as tractable as those who responded to the appeal of sentiment.

After the donor has been selected he is subjected to a thorough cross-questioning as to his family and personal history, and a thorough physical examination. This is for his own benefit as well as for the benefit of the patient, as in some cases it has been proven inadvisable to bleed the would-be donor.

In all the author's cases the regeneration of the blood lost by the donors was uninterrupted and rapid. This statement is based on their general appearance subsequent to losing the blood, their freedom of symptoms suggestive of the experience through which they had passed, and, more particularly, on the blood examinations made in as many cases as was possible under the particular conditions of each individual case. In no case was there anything but a temporary disturbance of the general functions. Apparently the return to normal varied directly according to the amount of blood lost—the more that was lost the longer the lapse of time before the return to the original amount.

The amount of blood which is allowed to pass from donor to recipient varies according to a considerable number of factors. These may be tabulated as follows:

1. The duration of the flow.
2. The size of the radial artery and the elasticity of its wall.

3. The blood-pressure of the donor.
    a. The normal pressure.
    b. The pressure as affected by psychic influences.
4. The method of making the anastomosis.
    a. The suture method.
        (1) The accuracy with which the suture is made (leakage, reduction of size of lumen).
    b. The cannula method.
        (1) The accuracy with which the connection is made (turning the tube sideways).
        (2) Adaptation of cannula to size of vessel.
        (3) The tension on whichever vessel passes through the cannula (see previous explanation).
        (4) Whether the vein or the artery passes through the cannula (on account of the varied thickness of wall).
        (5) The resistance offered by the vascular system of the recipient.

It is necessary to discuss but two of these factors here, as the others are discussed in appropriate places elsewhere. From the donor's standpoint the *duration of the flow* is an important consideration. The best way of determining when to stop the flow is by watching his symptoms. At first he will show loss of color in his mucous membranes, pallor of the skin, slight uneasiness, slight quickening of the pulse and respiration, lowering of the blood tension, and beginning shrinkage in the skin of the face. Progressive hemoglobin determinations often furnish a good index of the general condition, and may be easily made. All of the symptoms are progressive, and as soon as they are well marked the flow should be stopped. Often

the condition of the recipient will necessitate this long before the donor shows any symptoms at all. Definite rules cannot be laid down. Everything will depend on the judgment and experience of the surgeon. Temporary cerebral anemia can be readily controlled by changing the donor from the horizontal to the head-down position.

The approximate determination of the amount of blood which is lost can be made by carefully weighing the donor to fractions of an ounce before and after the transfusion. The conditions of the weighing must be the same at each time. It is futile to attempt to calculate the amount of transfused blood from direct observation of the loss of a few cubic centimeters in a given time from the radial artery. A few experiments have been done in the laboratory which showed how much the rate of flow varied as the flow progressed, and how useless the attempt was to obtain accurate calculated results.

That the blood-pressure may be markedly varied by reason of psychic influences has been repeatedly demonstrated by many different observers. It is largely for this reason that the elimination of disturbing influences at the time of the operation is so important. This is accomplished not only by the previous dose of morphin, but by the noiselessness of a perfectly equipped and smoothly run operating room.

A final point must be considered in regard to the protection of the donor against injury, and that is the possibility of his becoming infected from contact of his artery with the vein of the recipient in cases in which transfusion is performed for an infectious disease, and, more particularly, one which is acutely infectious. In the author's cases of hemorrhages in typhoid fever the donors were purposely chosen because they had had typhoid. The possession of immunity would in itself protect the donor in such a case as well as the un-

usual care taken to avoid exposure. The author believes that there is little or no risk in a chronic infection like tuberculosis or from an old septicemia or mixed infection. This is largely due to the fact that there is no chance for the blood being forced back from the recipient into the donor against the donor's arterial pressure. At the end of the transfusion there is a good margin of safety as regards any of the possible infection in the vein of the recipient being retained by the donor, as the donor's artery may be severed at least 2 cm. from the point of anastomosis. Moreover, the exposed tissues may be freely irrigated with corrosive sublimate in 1–2,000 solution. The exact amount of risk from this source must be very small, and with care as suggested it hardly seems likely that the danger of infection need ordinarily be feared. At all events, cases of acute infection rarely require transfusion.

THE RECIPIENT

The question as to what pathologic conditions may be suitably treated by transfusion of blood from one human being to another has not been definitely settled. The most that can be said at present is that it is clearly indicated in certain conditions and as clearly contraindicated in certain others. With our present knowledge the author feels that it should be used only when all other resources at command have failed.

Cases are on record in which transfusion was said to have been followed by recovery when in reality the patient died of the disease, and on the other hand deaths were said to have occurred from the disease when they should undoubtedly have been ascribed to accidents of transfusion.

As far as the recipient is concerned, transfusion is a prob-

lem in mechanics as well as in therapeutics. There are certain dangers which must be avoided under both of these headings, and in the recognition of their existence and their successful avoidance lies the responsibility of the surgeon. There are few if any operations in which more factors must be considered, and in which more care must be exercised.

From the mechanical standpoint the chief danger to be feared is acute cardiac dilatation and subsequent cardiac failure caused by transfusion in excessive amount or at excessive rate of flow. This danger is particularly great when the vitality of the patient is much lowered in the course of a severe illness, or when any previous functional or organic cardiac complication is present. Fortunately, as has been frequently shown in the author's series of cases, a certain amount of dilatation may occur and pass rapidly away without causing either immediate or subsequent harm.

The best treatment of acute cardiac dilatation is prevention. If the blood-pressure of the donor is high and his radial artery large, too rapid a flow may be prevented by partially narrowing the lumen of the artery with gentle pressure of the fingers. The effect can be gauged by the changes in the strength of the pulsation beyond the cannula in the vein. It may be necessary to shut off the flow altogether for short intervals, giving the heart a chance gradually to assume its added burden by allowing only small amounts of blood to pass across at a time.

As another means of prevention of acute cardiac dilatation, it may be necessary to bleed the recipient freely before transfusion. In cases of shock or of acute hemorrhage a preliminary bleeding would do harm. In many cases of subacute hemorrhage it is unnecessary. In all other cases either a preliminary bleeding must be performed or the amount of blood transfused must be much smaller than would otherwise be

possible, and the care taken correspondingly great. It should be remembered that reduction in the corpuscular elements in the blood of the recipient does not necessarily mean reduction in the fluid content (as, for example, in pernicious anemia), and also that where saline infusion would rapidly pass out of the vascular system blood will be retained. In cases where great weakness of the patient is associated with marked reduction of the red corpuscles it may be unsafe to bleed unless the bleeding be done at the same time that the transfusion is progressing.

Another phase of the mechanics of transfusion is the possible transudation of the blood into the tissues or body cavities with or without rupture of small vessels in the parenchymatous organs. This possibility may be disregarded in human beings as symptoms of cardiac distress will occur long before there is any danger of transudation.

The principal symptoms of acute cardiac dilatation are dyspnea, distress or pain in the precordial region, cough, and cyanosis. The pulse increases in rate and may be very irregular in action, tension, and volume. The right heart is chiefly affected. Percussion over the right border may give dullness extending out as far as an inch from the border of the sternum. Unless the strain on the heart is immediately relieved the increase in severity of the symptoms is rapid, and, if allowed to go too far, death will result. The rapidity with which a heart will dilate and return to its previous size is sometimes remarkable. This fact should never be counted on, however, as a means of getting out of difficulties brought on by over-transfusion.

When acute dilatation has once occurred it must be promptly recognized. The transfusion must be stopped, the operating table tilted so as to raise the patient to the head-up position, and rhythmic pressure made on the chest over the heart.

If recovery is not complete in a short time the transfusion should be given up, and the patient put to bed in a head-up posture, given carefully graded doses of nitroglycerin to insure peripheral dilatation of the vessels, and digitalin hypodermically *in very small doses* to stimulate the heart muscle directly. Small doses of morphin may also be given if needed, but it must be remembered that the recipient has had $\frac{1}{4}$ of a grain before the transfusion. Absolute rest and quiet and a reduction of the amount of fluids ingested are also requisite. Such a patient needs careful watching with treatment of the symptoms as they arise.

The treatment of shock and of acute hemorrhage by transfusion is primarily mechanical in its nature, and need not be discussed further here under the general considerations. The treatment of all other conditions, however, is a question of therapeutics when reduced to its final analysis. The surgeon takes the place of the internist when he gives a "dose" of blood.

In the therapeutics of transfusion there is a possible danger to be considered. In certain diseases, when similar bloods are intermingled (i. e., blood from animals of the same species, what is ordinarily designated as "hemolysis" occasionally occurs. Agglutination of the red corpuscles and precipitation may also occur, but, from a practical standpoint at least, the author has had no reason to believe that these two last changes may be regarded as possible sources of danger.

The mistake must not be made of considering "hemolysis" as destruction of the red corpuscles alone. It would be more appropriate to say that "hemolysis" is a toxic condition which gains its name from the fact that the red corpuscles are destroyed to a greater or less extent, but that *one* of the *effects* is not the cause. Hemolytic destruction of red corpuscles is one matter, but toxemia is another. The serum of the patho-

logic blood may act as a poison and incidentally destroy certain of the red corpuscles. When the amount is large, appreciable changes probably take place in the parenchymatous organs such as occur when dissimilar blood is transfused. It is a question as to whether the interaction of similar serum on the red corpuscles and on the other organs does not cause the formation of new toxic substances which were previously present in neither—i. e., that it is more than the poisonous action of the serum alone which must be held responsible. Moreover, may not a possible rôle of the leucocytes be overlooked when the red cells alone are considered?

The pathologic changes which follow injection of dissimilar blood have been studied by Hasse and his followers and others. The extent of the lesions varies considerably for a given animal, according to the species from which the blood is taken, serum from one species being more toxic than that from another; but the extent varies still more with the *amount* of blood transfused. It seems reasonable that there should be a direct ratio between the dosage and the effect produced, just as there is in giving a drug. While a small amount of a given enzyme will hydrolyze a disproportionately large amount of organic substance without losing its powers, there is no evidence of any similar action occurring between toxic serum and the blood or other cells of the recipient.

From the above it may be deduced that the question of dosage may be very important, especially when there is hemolysis of the recipient's red corpuscles by the donor's serum. Therefore, in all but emergency cases preliminary hemolysis tests should be made in order to handle a given transfusion more intelligently and protect the recipient more fully. The technic to be followed in making these tests is described in a following chapter.

The author has had but one case in which serious hemol-

ysis occurred. The patient had an inoperable suppurating carcinoma of the groin, and was transfused on three separate occasions from five different donors. The hemolysis began to appear on the second day after the third transfusion (from two donors). Death occurred ten days after this transfusion. After the previous transfusions there had been no gross evidences of hemolysis, although no tests were made to determine whether any hemolysis occurred or not. The question is whether death was due to hemolysis in the broader and more correct sense (i. e., from toxemia), whether hemolysis would have occurred if the two donors had been used on separate occasions instead of one immediately after the other, whether transfusion from either of the donors alone would have caused hemolysis, and whether death was due to hemolysis (toxemia) caused by the action of the cancer element in the serum on the blood from the donor.

It is impossible to say whether death occurred from hemolysis (toxemia from the transfused serum) alone or from a combination of causes. The patient was more or less septic from the presence of infection in the ulcerated cavity in the groin. He had had a long and severe illness, the bleeding before the transfusion was unusually severe, and while the blood lost was more than replaced it was a severe test of his strength and endurance. The cancer was hopelessly inoperable and had progressed well along toward the terminal stage. There had been no appreciable hemolysis after the other transfusions, and in several other cases patients had received blood from different donors without its occurring. It is known that cancer serum will hemolyze red corpuscles, and the hemolysis may simply have been due to the complete destruction of the corpuscles from the donor (the patient's blood must have been very largely substituted by the transfused blood) without toxin formation which would affect any of the patient's cells

(they were already more or less immune to the toxin liberated from the cancer). On the other hand, in patients in the last stages of cancer the author has found that a "reverse hemolysis" occasionally occurs—i. e., that the red cells from the cancer patient are hemolyzed by normal serum. That death was not due to asphyxia from destruction of the red corpuscles was shown by the fact that there were no symptoms before death which suggested asphyxia. The probability is that death was really due to a combination of factors which cannot be separated to estimate the exact influence of each. This case suggested the hemolysis test for cancer.

If it is found by the preliminary tests that the red corpuscles of the recipient are hemolyzed by the serum of the would-be donor, the advisability of transfusion should be carefully considered. This does not necessarily indicate that the blood of the donor is at fault, but rather that the recipient is in such a condition that any blood would be toxic to him when introduced into his circulation. In all cases which the author has had there has been no evidence that the blood of the donor was ever at fault. Therefore it is improbable that it would avail in such a situation as the above to try to use another donor. This is not meant to convey the impression that the blood of the donor may never be harmful in itself—in time donors may be found to whom the causation of harm may be traced. So far, however, this has not been done. On the other hand, if the serum of the recipient hemolyzes the red corpuscles of the donor, it does not necessarily mean that another donor should be chosen. It all depends on whether the effective principle or principles of the serum are altered at the same time that the red corpuscles are destroyed.

Following a successful transfusion certain phenomena almost always occur. The stimulating effects of the new blood

may be very marked. A poor surgical risk may be made a good one, the delirium of extreme hemorrhage or of toxemia may be replaced by a return to normal mental conditions, or the wrinkled aged face of prolonged hemorrhage may be restored to its normal aspect and the years apparently fall away under the very eyes of the observer.

A chill of greater or less severity followed by a corresponding febrile reaction is to be expected, and usually occurs. Former writers have often commented on this phenomenon. It is not necessarily an indication of hemolysis, although a violent chill is apt to follow transfusion of dissimilar blood. Ordinarily it apparently has no more significance than the chill which frequently follows the infusion of saline solution. In this connection it is of interest to note the observations of Debove and Bruhl, who found after giving saline infusion a rise of temperature of 1.5° C. (2.7° F.) in 19, 1° C. (1.8° F.) in 31, and 0.5° C. (0.9° F.) in 45 out of 95 cases.

The heart action is strengthened, the pulse becomes regular, slower, of higher tension and better volume, and the respirations slower and less shallow. In a hemorrhage case the change in the hue of the skin and mucous membranes may be very marked, while the red cells and hemoglobin increase in proportion as shown by the red counts. In a certain number of cases the recipient has vomited a small amount of watery grayish material. The actual case histories, however, should be consulted for the account of the changes occurring in the individual cases.

As with the donors, the question arises as to how much blood should be transfused. The condition of the donor and the recipient and the purpose of the transfusion enter into this. Here again very much depends on the judgment of the surgeon. No definite rules can be given. Enough blood must be transfused to accomplish as much good as possible, and yet

too much must not be given. Sometimes in cases where the patient does not suffer from the loss of a large amount of blood it seems to be as advantageous to transfuse small as large amounts. The symptoms of the recipient give the best key to the situation.

CHAPTER XVI

HEMOLYSIS AND ITS RELATION TO THE TRANSFUSION OF SIMILAR BLOOD

WHEN in 1899 Metchnikoff began to experiment on the hemolytic effect of organ extracts from different animals, he did so to prove, if possible, the theory that the process of phagocytosis is carried on by two distinctly differentiated classes of leucocytes. These two classes were the polynuclear leucocytes, to which the term "microphages" had been applied, and the mononuclear leucocytes, or "macrophages." The latter class were subdivided into "free" macrophages, found in the blood, and "fixed" macrophages, found in certain body tissues. Metchnikoff used the lymphatic glands of the omentum and the spleen of a guinea pig, and accidentally discovered that a saline extract of these glands possessed marked hemolytic activity.

From 1899 until 1901 little was done to advance this theory, when Trassevitch, of the Pasteur Institute, not only confirmed the results of Metchnikoff, but added the extracts of the pancreas and the submaxillary gland of guinea pigs, rabbits, and dogs to the list of extracts whose hemolytic activity had been proven. Up to that time they had been tested only against blood from animals of different species, but he for the first time tested them against blood from animals of the same species. His results were confirmed by Klein and Shigayama in 1901.

In the mean time, French scientists began to investigate the hemolytic activity of blood serum and tried to isolate the

"hemolysins" of both organ extracts and blood and prove them to be identical, when a new phase of the subject was introduced by Ehrlich at Frankfort. He promised to explain hemolysis in the same way that his side-chain theory explains immunity, and to disclose the origin of the disputed complement in the blood. In 1902 Morgenroth and Korchum published an elaborate paper on the hemolytic properties of organ extracts. They concluded that hemolysins of extracts could in no way be identified with those of blood serum, basing the differentiation largely on the action of heat on the different substances in question. They made one great advance in showing that organ extracts were active not only with the red cells of the same species of animals, but also the red cells of the same individual from which the organs had been derived.

From the hemolytic activity of organ extracts the interest shifted to tumor extracts and to the cause of the typical symptoms of cachexia and secondary anemia which appear in patients suffering from malignant diseases. That this condition was due to a toxin circulating in the blood was quite universally believed, because of the occurrence of urobilinuria in certain cases of malignancy and the great resistance of the red cells to anisotonic salts in certain advanced cases of malignancy.

The hemolytic activity of tumor extracts was first tested by Hans Sachs, in January, 1902. This was followed in the next year by the experiments of Micheli and Donati. The results in all these tests were as varied as the types of tumors examined. In 1904 an elaborate paper was published by Kellman. It was full of theories and misconceptions, and cannot be accepted at all in the light of later investigations, but must receive mention from the fact that it gave a much needed stimulus to the work and caused a wider spread interest than had previously existed.

Within the last two years Beebe, of New York, has

added much valuable material to the problem of cancer research, which at the present time includes the study of hemolysis, and with the aid of Richard Weil has made many experiments on the hemolytic activity of tumor extracts in all stages of the disease. He has found that tumor extracts have marked hemolytic activity, and that this is especially true of the saline extracts of necrotic tumors. He has also shown that the blood, as a whole or in part, as serum or red cells, plays an important part in increasing or limiting the hemolytic activity of tumor extract.

Gay and Ayer, of the Danvers, Massachusetts, Institution for the Insane, have recently published a series of experiments with blood from rabbits and cows, to observe if possible any toxic changes in the blood of patients suffering from different forms of insanity, but they found no definite facts of clinical value.

It has recently been shown that substances behaving like antitoxic and bacterial substances can be produced in the tissue fluids by the injection into the animal of various substances other than bacterial toxins or bacteria. Included among these substances are the red cells of an animal of a different species to that from which the corpuscles are derived, their destructive action being shown by the red cells of the recipient being no longer capable of retaining hemoglobin, the latter leaving the red cells to become dissolved in the serum.

Red blood corpuscles are composed of a capsular membrane filled with protoplasm. The membrane consists chemically of three substances—phosphorized fat, a monatomic alcohol cholesterin, and a nucleo-proteid. During its life it can prevent the escape of hemoglobin, which occurs on death of the cell. All protoplasmic poisons kill the membrane and cause hemolysis, because the osmotic pressure of serum is a little less than that of the cellular contents. Physiologists

have long recognized that repeated freezing and thawing of blood and the addition of certain chemicals will cause hemolysis. In the case of biological or chemical poisons there is something which causes a change in the envelope of the red cell and increases its permeability.

Baumgarten has noticed that the first stage of hemolysis, as produced by a biological poison, is a swelling of the corpuscles—just the condition which occurs when the serum is made hypisotonic. After heating, hemolytic serum is made hypisotonic. Heating hemolytic serum to 55° C. does not in any way influence its osmotic pressure, but does destroy its hemolytic activity. From this it seems safe to suppose that the hemolysin increases the permeability of the envelope, and the slight anisotonic condition of the corpuscles and serum is then sufficient to cause a diffusion of hemoglobin. Landau, from microscopical observations, finds no change in the cell nucleus, but only a purely mechanical change in the cell wall.

Hemolysis also may be caused by disturbance of the osmotic pressure. So long as the osmotic pressure of the fluids in which the red cells are suspended is almost the same as that of the corpuscular contents (that is, of the same molecular concentration, or "isotonic"), and the envelope is uninjured, no hemolysis occurs. If, however, the osmotic pressure of the surrounding fluid is less than that of the corpuscles (hypisotonic) the corpuscles absorb water, become swollen, and ultimately let free the hemoglobin. This law of osmotic equilibrium does not, however, hold true for all salts or neutral bodies. Ammonium salts, in whatever concentration, cause laking of blood. The same is true of urea.

One must distinguish clearly between the two classes of hemolytic agents—those which poison the envelope but do not alter the osmotic relationship of the corpuscles and the serum, and those which primarily alter the isotonic conditions so that

certain molecules (water) diffuse into the corpuscles, causing the latter to distend and to liberate the hemoglobin.

It is to Bordet that we owe the discovery of hemolysins. He proved by a conclusive series of experiments that hemolysis is specific in its action, and formulated a law as follows: The blood serum of an animal of Species A acquires the property of causing hemolysis of the red cells of Species B (and, to a less extent, of the other species of the same genus as B) when that animal is repeatedly treated with the blood of Species B. Intraperitoneal, subcutaneous, and intravenous injections of blood, and the feeding of an animal with the blood of another species, will cause hemolysis. Hemolysis may also be produced in the vessels of an animal by the injection of specific hemolysins. This was done by Bordet, and his results were confirmed by similar experiments by Balfanti and Carbone.

At this point in the discussion a general summary is practically this: An organism is normally endowed with a certain amount of destructive power toward all cells foreign to its tissues. This power (cytolysis) may be increased in any animal by the repeated injection into it of non-lethal but gradually increasing doses of suspensions or extracts of these foreign cells. The increased cytolytic power which results depends not on an increase in the destructive power of the agency, but on the development in the tissue fluids of a substance which increases the sensitiveness of the invading cells toward the normally existing destructive agency of the tissues.

Bordet's attempted explanation of bacteriolysis and hemolysis was not satisfactory, and it is to Ehrlich and Morgenroth that we owe a conception which seems to explain all the facts. The well-known "side-chain theory," with which all students of bacteriology are familiar, seems to most scientists to be an adequate explanation of the phenomena. As a preliminary

step toward this theory, Fodor and Nuttal showed that fresh blood of various animals has the power of destroying bacteria, and later Bucher showed that blood serum from a spontaneous clot has all the bactericidal properties of the whole blood. Metchnikoff, on the other hand, demonstrated the phagocytic action of the leucocytes over bacteria, thus showing the important defense possible in the body against bacterial invasion. The increase in the hemolytic activity of the serum seems to correspond with the increased " alexin " content of the human serum, as worked out by Metchnikoff, Bordet, and Gengou, as its maximum activity takes place after twenty-four hours' standing on a spontaneous clot at 0° C., which corresponds with the time of disintegration of the leucocytes.

From all these controversies between the enthusiasts of either the humeral or the cellular theory of immunity, it must be recognized that the essentials are not antagonistic but reciprocal. The " alexin," or active fermentlike body of Bucher and of Bordet, is equivalent to the " complement " of Ehrlich, and the " amboceptor " of Ehrlich is no more or less than the " substance sensibilisatrice " of Bordet and the immune body of Buchner, and that these bodies are present in normal as well as pathological serum is an established fact. From all these parallels the two theories of immunity have been evolved, the physico-chemical theory of Bordet and the purely chemical theory or hypothesis of Ehrlich. That neither has been finally accepted by all experimenters makes it equally impossible to apply either in all cases of hemolysis, but either will form a good working basis for the clinician as well as the scientist.

Hektoen has recently confirmed the findings of Landsteiner and Descatello and Sturli in regard to the separation of human beings into three groups, according to the agglutinating reaction of their blood. Group I is composed of those indi-

viduals whose red corpuscles are not agglutinated by the blood sera of Groups II and III, but whose sera agglutinate the corpuscles of Groups II and III; Group II, of those whose corpuscles are agglutinated by the sera of Group III (and Group I), and whose sera agglutinate the corpuscles of Group III, and finally Group III of those whose corpuscles are agglutinated by the sera of Group II (and Group I), and whose sera agglutinate the corpuscles of Group II. Of the 76 persons whose blood he studied, Hektoen found 36 belonging to Group I, 26 to Group II, and 14 to Group III. Of the 14 in Group III, 6 were without any agglutinin, so that about 90 per cent of the individuals possessed isoagglutinins of one kind or another. He states that there is no striking alteration in the agglutinative grouping of persons with various diseases, more particularly pneumonia, typhoid fever, scarlet fever, and advanced pulmonary tuberculosis.

As regards the nature of the agglutinins, they apparently have special affinities for the corpuscles on which they act. They vary in amount in different individuals. They are stable bodies—they resist heating to 60° C. for thirty minutes, pass through porcelain filters, and persist for months in serum kept in the ice box.

Hektoen concludes that "the occurrence of isoagglutinins in human blood suggests that under special conditions homologous transfusion might prove dangerous by erythrocytic agglutination within the vessels of the subject transfused." As they have not been found in the sera of suitable animals, it has not been possible to conduct experiments tending to prove this theory.

At the present time we are probably only on the boundary line of knowledge concerning the different constituents of the blood and their reactions. Moreover, what is apparently true to-day may be contradicted to-morrow, so that we cannot feel

very sure of our ground until more research work has been undertaken and the results tested by time.

TECHNIC OF MAKING HEMOLYSIS TESTS

In collaboration with Miss O. M. Lewis and Dr. A. M. Tweedie.

Owing to the many extraneous factors which may modify the results, it is difficult to secure reliable hemolysis tests. Among these factors may be mentioned contamination of the blood with organic or inorganic substances which in themselves will hemolyze it, changes in the temperature at which specimens are kept, mechanical injury of the corpuscles themselves, and the fact shown by experience that when the blood corpuscles are separated from the serum by centrifugalizing, or by drawing the blood into sodic citrate solution, the hemolytic action is either lessened or prevented. Another important factor is the change in intensity of the hemolytic reaction with the passage of time—the maximum activity occurring in about twenty-four hours in serum which has been obtained by allowing the blood to clot.

Comparison of the reaction of the blood from the patient whose blood is being examined is made by suspending normal red cells in the patient's serum and red cells from the patient in normal serum. That blood from supposedly normal persons is actually normal can only be determined by hemolysis tests. Before comparing the blood of a patient with an assumed standard it is necessary, therefore, to test the standard. Moreover, if blood from several supposedly normal individuals is compared with that of each as well as with that from the patient, but very slight chance for error remains.

As a further precaution toward securing absolute accuracy of results the fact is taken into consideration that organic

hemolysins from the human body are destroyed by heat while inorganic hemolysins from extraneous sources are not. A temperature of 55° C. for ten minutes destroys all such organic hemolysins. So far as they have been studied by the author, the hemolysins of disease are organic. If, then, all the specimens of blood in any given test are prepared in duplicate and one set is subjected to a temperature of 55° C. for ten minutes, possible error due to contamination with extraneous inorganic hemolysins may be avoided.

The apparatus required for making hemolysis tests is as follows: (1) Incubator, (2) refrigerator, (3) sterilizer, (4) one gross of ordinary $\frac{1}{2}$-inch test tubes, (5) 32 tubes $3 \times \frac{1}{4}$ inches (the latter dimension the inside diameter), (6) test-tube racks made to hold 72 tubes, each aperture being numbered consecutively in any permanent way, (7) glass beads for defibrinating the blood, and, finally, (8) several aspirating needles with stylets.

The instruments should be cleansed in distilled water. The smaller tubes should be kept immersed in sterile isotonic sodic chlorid solution, and taken out only when they are used. The large tubes are used in pairs for each individual, one for obtaining the blood for the red cells and the other the blood for the serum. In the tube for the cells a glass bead is placed. These tubes are closed with stoppers of absorbent cotton wrapped in close-meshed cotton cloth, sterilized, and set aside for later use.

The blood for the tests is obtained from a superficial vein in the arm—usually the median basilic vein at the elbow. The skin of the operative field is scrubbed with soap and water, and then with sterile water, or, better, sterile saline solution. Above the operative field the arm is compressed with a bandage applied so as to obstruct the venous flow and dilate the vein from which the blood is to be removed. The

needle is then inserted into the vein through the skin—an easy matter after a little experience. No local anesthetic is required.

Three cubic centimeters of blood is drawn into the tube with the bead, which is then immediately and continuously agitated for ten minutes. This defibrinates the blood. Into the other tube 10 c.c. of blood is drawn. This tube is kept at rest in a slanting position while the blood separates into clot and serum.

Before the needle is withdrawn from the arm, unnecessary oozing may be avoided by removing the bandage.

The further preparation of the blood consists in transferring the defibrinated blood into a tube containing 20 c.c. of 0.85 per cent saline solution (made up with distilled water). The latter and the tube containing the clotted blood are placed in the refrigerator for approximately twenty-four hours. Cold facilitates clotting and preserves the blood by inhibiting any possible bacterial activity. At the end of this time the separated serum is carefully pipetted off, put into another sterile tube, and again replaced in the refrigerator. At the same time the supernatant fluid in the tube containing the blood is poured off, and 20 c.c. of fresh isotonic saline solution is added. When needed this mixture is gently shaken until the cells are in complete suspension.

All of the above process is carried through with blood from the patient and from three supposedly normal individuals.

The experimenter then has the corpuscles and serum from four individuals—the patient, A, and three supposedly normal individuals, B, C, and D, respectively. Using the smaller tubes, $\frac{1}{2}$ c.c. of the serum of each person is put into each, and duplicate tubes are also prepared. One set is subjected to a temperature of 55° C. in a water bath for ten minutes. This

set is then placed in the refrigerator until cooled to the same temperature as the others. After the cooling the tubes are all taken from the refrigerator. Testing the patient's blood requires the addition in each case of $\frac{1}{2}$ c.c. of suspension of red corpuscles as follows:

Tube 1	Serum A	+ cells of A	Tube 17	Serum B	+ cells of C
2 (heated)	“ A	“ “ “ A	18 (heated)	“ B	“ “ “ C
3	“ B	“ “ “ B	19	“ D	“ “ “ D
4 (heated)	“ B	“ “ “ B	20 (heated)	“ D	“ “ “ D
5	“ B	“ “ “ A	21	“ D	“ “ “ A
6 (heated)	“ B	“ “ “ A	22 (heated)	“ D	“ “ “ A
7	“ A	“ “ “ B	23	“ D	“ “ “ B
8 (heated)	“ A	“ “ “ B	24 (heated)	“ D	“ “ “ B
9	“ C	“ “ “ C	25	“ D	“ “ “ C
10 (heated)	“ C	“ “ “ C	26 (heated)	“ D	“ “ “ C
11	“ C	“ “ “ A	27	“ A	“ “ “ D
12 (heated)	“ C	“ “ “ A	28 (heated)	“ A	“ “ “ D
13	“ C	“ “ “ B	29	“ B	“ “ “ D
14 (heated)	“ C	“ “ “ B	30 (heated)	“ B	“ “ “ D
15	“ A	“ “ “ C	31	“ C	“ “ “ D
16 (heated)	“ A	“ “ “ C	32 (heated)	“ C	“ “ “ D

The tubes when thus prepared are placed in the thermostat at 37.5° C. for two hours. Then they are placed in the refrigerator for twenty hours. At the end of this time the presence of hemolysis may be determined by the pink discoloration of the supernatant fluid and the condition of the cells in the sediment. The results are best read off by persons who have no knowledge of the identity of the tubes.

In general, it may be said that absolute accuracy must be followed not only in carrying out the technic, but in keeping the notes. Almost innumerable changes have been made in developing the technic to the present point, and the results obtained by its use are now fairly constant.

In the interpretation of results and their clinical application, experience has shown that the occurrence of hemolysis

in vitro before transfusion does not necessarily indicate that it will occur in the vascular system of the recipient after transfusion. The fact is once more emphasized here that our knowledge of hemolytic reactions and of their significance is still in a very rudimentary stage. This discussion on blood reactions and immunity is introduced for the double purpose of calling attention to the possibility of *dangerous reactions* and *suggesting therapeutic possibilities in the transference of immune bodies to combat certain diseases.*

THE CLINICAL APPLICATIONS OF TRANSFUSION

The following cases include illustrative cases taken from the literature as well as those of the author. The author's cases (55 patients on whom 61 transfusions were performed) have been grouped according to the condition for which the transfusion was primarily performed. For example, in Case No. IX, 1 (6,411), the patient was first transfused for acute hemorrhage following nephrotomy, but later was transfused again for acute pathologic hemorrhage from the bladder wall. On the second occasion the lost blood was not only replaced, but the bleeding was checked at its source. Again, a patient with exophthalmic goiter and carcinoma of the breast was transfused for neither, but to improve her general condition before the second of the two operations which she underwent. Several patients with chronic suppurative processes were transfused, but with part of them the transfusion was primarily to overcome postoperative shock, the treatment of the suppuration being a secondary consideration.

Up to a certain extent the negative results of former investigators have been disregarded in the hope that they might have been due to some other reason than failure of transfusion itself. Unfortunately, they have only too clearly been confirmed in part. In certain diseases there is evidence that beneficial results may eventually be obtained.

CHAPTER XVII

PERNICIOUS ANEMIA

(*Group I*)

CASE NO. I, 1 (6,700). ABSTRACT. CONSULTATION WITH DR. J. H. LOWMAN.

Pernicious Anemia; Transfusion; Death Thirteen Days after Transfusion.

The patient was an American woman, fifty years of age, who had complained of weakness during the two previous years. The diagnosis of pernicious anemia had been made, and she had received medical treatment during that time. At the time of admission it was decided to try transfusion as a means of last resort. This was done after careful consideration of the matter in consultation with Dr. Lowman. In spite of his treatment the disease was steadily progressing, and the patient seemed to be in a hopeless condition.

The patient was fairly well nourished. She had the characteristic lemon-yellow color, and was very weak. The heart was normal in size. A soft systolic murmur could be heard at the apex. The day before the transfusion the blood examination showed marked poikilocytosis, polychromatophilia, and no nucleated red cells. Two days previously 134 normoblasts and 18 megaloblasts were seen in a differential count of 500 leucocytes. There were 804,000 red cells per cubic millimeter, 2,600 whites, the hemoglobin was 15 per cent, the blood platelets were reduced to 44,700, the specific gravity was 1.031, the coagulation time four minutes and thirty seconds, the color index 1.09, and the blood-pressure 105 mm. of mercury.

The donor was the patient's husband. His left radial artery was anastomosed to the left median basilic vein of the patient by the suture method. The blood was allowed to flow across for forty-five minutes.

Just after the transfusion the patient showed signs of acute dilatation of the heart. She was propped up in bed and given digitalis. Otherwise the immediate effect of the transfusion was to improve

her condition—she was stronger, her color was better, and she gradually lost her lemon tint. The red count had risen to 1,280,000, the hemoglobin to 25 per cent, the white count to 4,800, and the color index was 1.0. The specific gravity was 1.027, the blood platelets 55,666, the coagulation time two minutes and thirty-one seconds, and the blood-pressure 110 mm. The stained specimens presented about the same appearance as at the last time, with the exception that more normal red cells were present. Three normoblasts and one megaloblast were found after half an hour of search. No evidence of hemolysis was found either in the blood drawn or in the symptoms of the patient. The acute dilatation gradually cleared up under the treatment described above.

The first day after the transfusion the red count was 1,176,000, the white count 3,600, the hemoglobin 25 per cent, and the blood-pressure 115 mm.

The second day after the transfusion the patient's temperature rose to 102.3° F. A cough without expectoration developed, some dullness was found over the bases of the lungs posteriorly, and moist râles could be heard in the same areas. There was probably bronchopneumonia with edema, but the diagnosis was not made with certainty. The temperature fell to normal in two days.

The fifth day after the transfusion the red count had fallen to 928,000, the hemoglobin to 15 per cent, the white count to 3,600, and the blood-pressure was 125 mm.

By the eighth day the hemolysis had progressed still further, the red count being 784,000, the hemoglobin 15 per cent, the white count 2,600, and the blood-pressure 110 mm. After this the patient gradually sank, and on the thirteenth day after the transfusion death occurred, with the clinical signs of edema of the lungs present. An autopsy was not held.

Comment.—It would have been better to have bled the patient as freely as possible before and during the transfusion. The tissues were already surcharged with fluid throughout the entire lower part of the body. Destruction of the red cells does not imply a diminution in the fluid constituents of the blood, and hence the circulation was overloaded by the addition of so much new blood. As it happened, this caused only temporary embarrassment, which was doubtless accentuated by the heart itself sharing the general muscular weakness pe-

culiar to the disease. It plainly showed the necessity of being very careful not to overload the circulation in any such case.

The effect of the new blood in modifying the course of the disease was absolutely negative. The new corpuscles were

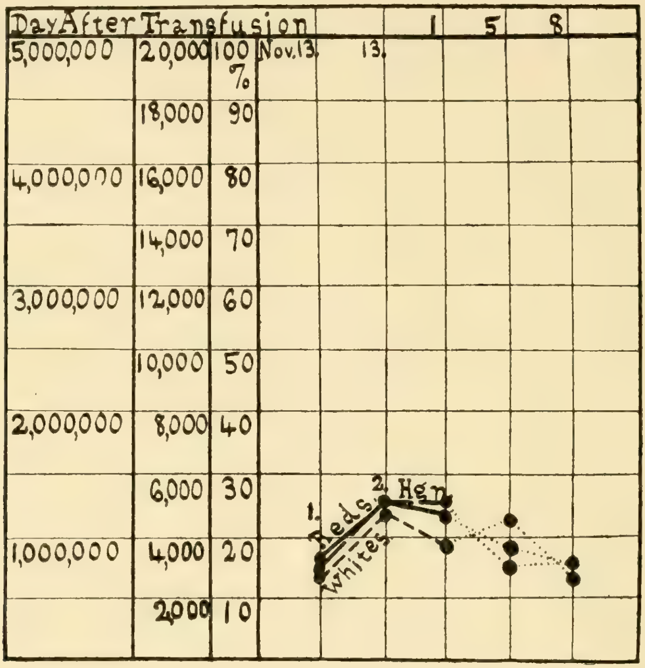


FIG. 46.—CASE NO. I, 1, (6,700). BLOOD CHART OF RECIPIENT. PERNICIOUS ANEMIA. 1, 2. Just before, and just after transfusion. Duration of transfusion, forty-five minutes. Note rapid hemolysis of the new blood.

rapidly destroyed, as shown by the fall to the original number in about five days. It was evident that there was an active hemolyzing agent at work. The fact suggests itself that the reason, at least in part, why all the corpuscles in the patient's blood are not rapidly destroyed by whatever the hemolyzing agent may be, is that there is a gradually acquired partial immunity. The production of the toxin is slow, and

time is afforded for the establishment of a certain amount, but not sufficient immunity to save the patient. Apparently death finally occurs from lack of sufficient red cells to carry on the distribution of oxygen to the tissues, rather than from poisoning. The transferred red cells were thrown suddenly in contact with the hemolyzing agent, and had no time to acquire immunity.

As the statistics of this case are given above they are not repeated in tabular form (see Chart, Fig. 46).

Case No. I, 2 (6,706). Abstract. Consultation with Drs. C. F. Hoover and H. G. Wagner.

"Sciatica"; Enlarged Liver and Spleen; Rapid Autolysis of Unknown Origin; Severe Hemorrhage from Nostril; Transfusion; Temporary General Improvement; Rapid Hemolysis of New Blood and Return to Condition Present before Transfusion; Death Seven Days after Transfusion.

The patient was an American woman, twenty-nine years of age, who complained of weakness.

Family History.

1. Mother's Family.—The mother's mother died of pneumonia. She did not show any tendency to bleed abnormally. The mother's father died of apoplexy. He also did not show such a tendency. The mother's first brother died of Bright's disease. The only record of bleeding in connection with him was in an operation in which he had a severe loss of blood. The nature of the operation was not stated. The mother's second and third brothers had hemorrhoids, and the latter had had considerable nosebleed in earlier years. The mother's four sisters all had hemorrhoids and a tendency to bleed easily. One of them flowed very severely at her change of life.

2. The Mother.—The mother had always bled freely in the course of her life, especially from her nose and from hemorrhoids.

3. Father's Family.—The father's father died of pulmonary disease. The father's mother died of a "paralytic stroke." The father's brother died of tuberculosis. The father's two sisters were living, but had no signs of pulmonary tuberculosis. One of them showed a tendency to bleed easily.

4. The Father.—The father died of Bright's disease. He had bleeding hemorrhoids until he was thirty-five years old.

5. The Brothers.—Four brothers of the patient were living. They all were hemorrhoidal, and all were given to bleeding freely.

6. The Sister.—The sister died of pneumonia.

Personal History.

The patient had had parotitis at eighteen years of age, and was quite sick. She had had no other illness. Her nose had always bled from slight traumatism. She had hemorrhoids, but said they seldom bled. Her periods were always regular, associated with considerable pain, and usually lasted for a week. She had been married two and a half years previously, and had one child, fifteen months old. She had never had a miscarriage. At the time her child was born the bleeding was normal. She had used a great deal of coffee, and occasionally alcoholic beverages. Her usual weight was 133 pounds. She had always had "black and blue" spots after slight traumatism.

Present Illness.

About six weeks before entering the hospital she "took cold" and had pain in her back and right sciatic nerve. The urinary analysis was negative. The pain persisted and got worse. With it she had slight fever. A few days later she had a few subcutaneous hemorrhages on her legs, which were thought to have been caused by her pinching the skin. At this time the heart and lungs showed nothing abnormal. The abdominal examination was negative, except for slight tenderness in the left inguinal region. Her skin as a whole had a grayish hue, and suggested that she was more seriously ill than the physical findings indicated.

Eight days before the transfusion she had intense pain, tenderness, and heat over the right sacroiliac joint, for which it was necessary to give her morphin. Her abdomen was considerably distended. The spleen was not palpable. Her temperature varied between 99° and 100° F.

Six days before the transfusion her temperature was practically the same. The abdominal distention persisted in spite of turpentine stoups, enemata, and the use of the rectal tube. The tongue was slightly coated. The inflammation of the sacroiliac joint had disappeared. There was some tenderness under the right symphysis pubis. Examination of the blood showed that it was normal in appearance. The red count and hemoglobin were apparently normal. The red cells were normal in size and outline, and formed rouleaux. No counts were made. A stained preparation showed no nucleated cells or other marked changes from the normal. The urine had a specific gravity of 1.027, high color, no sugar, and a trace of albumin.

Three days before the transfusion blood was taken from the ear for a Widal test. Bleeding continued from the puncture for fifteen minutes, and required hot applications to stop it. The test was negative, and the blood used did not coagulate for twenty minutes. The pain over the sciatic nerve was less intense.

Two days before the transfusion the patient's nose began to bleed at 10 A.M., and kept on bleeding until 9 P.M., in spite of plugging the nares. About a pint of blood was lost. The pulse rose to 130 per minute. A loud systolic murmur was heard over the apex of the heart, and the pulmonic second count was accentuated. The heart was not enlarged. For the first time the spleen could be palpated at the costal border. The edge was smooth and rounded, and neither hard nor sensitive. The abdomen was less distended.

The day before the transfusion the patient was examined by Dr. C. F. Hoover. She lay quietly in bed, and seemed to be very weak. Her skin and mucous membranes had a marked sallow pallor. There was no eruption, and no ecchymoses could be found. The pupils were equal, and reacted to light and to accommodation. The sclera were of a slightly yellowish tinge. The conjunctivæ were pale. The tongue was dry and tremulous, and heavily coated with a yellowish white fur. The throat was negative. The teeth were in good condition. The right nostril had the packing in place, and was not bleeding. There was no general glandular enlargement. The lungs were negative. The respirations were shallow and quiet, and at the rate of 24 per minute. The maximum cardiac impulse was seen and felt in the fifth interspace, 9 cm. from the midsternal line. The nipple line was 8.5 cm. from the midsternal line. The right heart extended 3.5 cm. from the midsternal line in the fourth interspace. At the apex there was a fairly loud systolic murmur. The second sound was clear. The murmur was loudest over the pulmonic area. The pulmonic second sound was accentuated. Over the aortic area the systolic murmur was soft. The aortic second sound was not loud. The veins of the neck were considerably engorged. In the jugulars there was a positive venous pulse. The radial pulse was regular, of good volume, easily compressible, and at the rate of 132 beats per minute. The vessel wall was palpable. The upper border of the liver was at the sixth rib, and the lower border was 3 cm. below the costal margin. The edge was sharp, soft, and palpable on inspiration. The spleen was enlarged to the costal border, palpable on inspiration, and soft. The abdomen was soft, not distended, not tender, and no masses could be felt. The shins were not edematous. The knee jerks were exaggerated. There was a suggestion of ankle

clonus, but no Babinski reflex was elicited. It was very evident that something was causing a marked destruction of the red corpuscles, as was confirmed by the blood examination made the next morning just before the transfusion.

The morning of the day on which the transfusion was performed the red count was 1,076,000, the hemoglobin 22 per cent (Haldane), and the white count 22,000. The coagulation time was four and a half minutes. The red cells showed considerable variation in size. On the average they were smaller than normal. There was little variation in their shape. A number of nucleated red cells were seen, mostly normoblasts. On the whole the blood picture was in striking contrast to what it had been at an earlier date. There was also recurring nosebleed. While there was no proven ground on which transfusion could be based, the failure of other treatment, the nosebleed, and the serious general condition seemed sufficient indications.

The patient's husband served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method. The blood was allowed to flow across for thirty-four minutes.

The immediate effect of the transfusion was striking. The pale, sallow cheeks became pink, the lips showed more color, and the patient was bright and talkative, and apparently felt stronger. In the morning, before the transfusion, Dr. Lenker had removed the packing from the nostril, with the exception of a posterior plug. The oozing at once started, and as he was unable to control it with adrenalin he was obliged to repack. During the transfusion the packing was all removed, and no more bleeding occurred. While the ear bled freely when blood was drawn for the examinations, there was no difficulty in stopping the flow. The red count had risen to 1,208,000, the hemoglobin to 30 per cent, and the white count had fallen a little to 21,040. By the next day the red count had risen to 1,608,000, but after that it steadily fell.

The patient retained her new strength for about two days, but then gradually lapsed into a very weak, drowsy condition. On the third and sixth days the stools gave a positive reaction for occult blood with the benzidin test. She had a deathlike sallow pallor, the mucous membranes being of about the same color as the skin. The spleen remained palpable at the costal margin, as did the liver. The heart gradually weakened and dilated, especially the right heart, and the venous pulsation in the neck became more marked. The lungs remained clear except for a few moist râles at the left base. The reflexes remained about the same. She had some aching in her

limbs, but no especial tenderness. The temperature began gradually to rise, finally reaching 105° F. She soon sank into coma, so that for the last twenty-four hours it was impossible to rouse her. Death occurred at about 11 P.M., seven days after the transfusion. A blood culture showed no growth. Permission could not be obtained to hold an autopsy.

Comment.—Drs. Hoover and Wagner thoroughly investigated the clinical problems of this case, but no satisfactory conclusion as to the cause of the rapid autolysis was reached. The transfusion was followed by the usual improvement in the patient's condition, but the new blood was hemolyzed within three days, so that the patient's blood was in the same condition that it was before the transfusion. As in the cases of

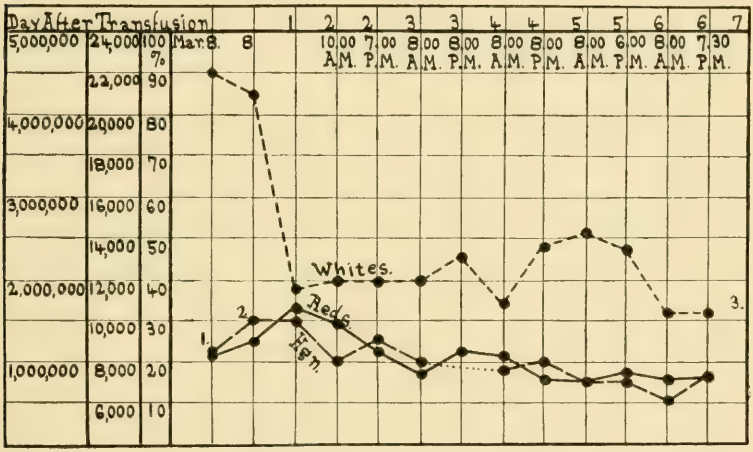


FIG. 47.—CASE NO. I, 2 (6,706). BLOOD CHART OF RECIPIENT. ACUTE AUTOLYSIS OF UNKNOWN ETIOLOGY. 1, 2. Before and after transfusion. 3. Death. Duration of transfusion, thirty-four minutes.

pernicious anemia on record in these pages and elsewhere, the transfusion appeared to exert no favorable influence toward stopping the autolytic action. For this reason it is included in this group.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Before transfusion.	1,076,000	22%	22,000
After transfusion.	1,208,000	30%	21,000
1st day.	1,608,000	30%	11,500
2d day.			
10.00 A.M.	1,444,000	20%	11,900
7.00 P.M.	1,116,000	25%	11,800
3d day [1]			
8.00 A.M.	816,000	20%	11,800
8.00 P.M.	1,112,000	....	13,100
4th day.			
8.00 A.M.	1,052,000	18%	10,800
8.00 P.M.	776,000	20%	13,500
5th day.			
8.00 A.M.	748,000	15%	14,100
6.00 P.M.	792,000	15%	13,400
6th day.			
8.00 A.M.	768,000	10%	10,200
7.30 P.M.	800,000	15%	10,200

(See Chart, Fig. 47.)

The red corpuscles showed marked variations in size, the average being smaller than normal. There was some variation in shape, but poikilocytosis was not at all marked. Many of the cells showed numerous fine punctate basophilic granules. The areas of central pallor were not much enlarged, but the achromia of the entire cells was in proportion to the hemoglobin estimation.

Tests for Hemolysis

Under rigid asepsis, washed corpuscles of the donor were mixed with serum of the patient and incubated. Before the

[1] On this day the differential count was as follows:

Polymorphonuclear leucocytes.	400	75.7%	Nucleated red corpuscles.
Small mononuclear forms.	95	18.0%	Normoblasts......58
Large mononuclear forms.	16	3.3%	Megaloblasts......17
Myelocytes.	14	2.6%	Microblasts....... 4
Eosinophiles.	1	0.1%	—
Mast cells.	11	0.3%	79
	537	100.0%	

incubation there was no hemolysis, but after incubating overnight there was a marked change, the serum becoming red. Stained smears showed shadow corpuscles. As a control the same process was repeated, using serum from a healthy man in one of the wards instead of that of the recipient. The results were entirely negative, no change occurring.

SUMMARY

CASE No. I, 1 (6,700).

Transfused.—For pernicious anemia.

Immediate Result.—Slight temporary improvement.

Other Treatment.—None.

Late Result.—New blood rapidly hemolyzed. Death thirteen days after transfusion.

CASE No. I, 2 (6,706).

Transfused.—For rapid autolysis of unknown origin, and persistent hemorrhage from nose.

Immediate Result.—Temporary general improvement; cessation of hemorrhage.

Other Treatment.—Inconsequential.

Late Result.—Rapid hemolysis of new blood. Death seven days after transfusion.

CASES FROM OTHER SOURCES

CASE A.—WATTS.[1]

Pernicious Anemia; Transfusion; Death Four Days Later.

The patient was a male, forty-four years of age, who was in an advanced stage of pernicious anemia. The donor was a man with polycythemia, whose red count was 8,712,000, and hemoglobin 123

[1] A synopsis of this case appeared in the Johns Hopkins Hospital Bulletin, 1907, May, p. 166, Case IV. The statistical details were kindly given by Dr. Watts in a personal communication.

per cent. A radial artery of the donor was anastomosed to a median basilic vein of the patient by the suture method. The blood was allowed to flow across for eighty minutes. At the end of this time the blood was found to be flowing from the artery at the rate of 16 c.c. per minute. It was thus estimated that the patient received at least 1,280 c.c. of blood. At the end of the transfusion there was a perceptible flush in the patient's face, conjunctivæ, and finger nails, but there were no marked changes in his subjective symptoms. The red count was found to have risen from 848,000 to 1,880,000, the hemoglobin from 23 to 38 per cent, and the white count to have fallen from 8,040 to 7,480. The new blood was steadily and rapidly destroyed, and death occurred four days later.

The statistics of this case are as follows:

March 15, 10 a.m.

Reds	816,000	
Hgn	23%	(Sahli, corrected.)
Whites	3,920	

Differential Count (500 *cells*)

Eosinophiles	12	2.4%
Small mononuclears	190	38.0%
Large mononuclears	90	18.0%
Polymorphonuclears	198	39.6%
Transitionals	9	1.8%
Myelocytes	1	0.2%
	500	100.0%

Nucleated reds seen in making the above, 25

Normoblasts	19
Intermediates	5
Megaloblasts	1
	25

March 25, 1907. Before the transfusion.

Reds	848,000	
Hgn	22%	(Sahli.)
Whites	8,040	

March 25, 1907. After the transfusion, 4 p.m.

Reds	1,880,000	There was no change in the general feelings.
Hgn	38%	There was a perceptible flush to the face, conjunctivæ, ears, and finger nails.
Whites	7,480	

March 26, 1907, 9.00 a.m.
Reds.......... 1,370,000
Hgn........... 28%
Whites........ 5,520

In the fresh blood there was poor rouleaux formation, and marked poikilocytosis, although many well-formed cells of normal size were found. No normoblasts were seen.

March 26, 1907, 4.30 p.m.
Reds.......... 1,384,000
Hgn........... 25%
Whites........ 6,480

In the fresh blood there was marked poikilocytosis. Many microcytes, and fewer macrocytes were seen. No normoblasts were seen.

March 26, 1907, 10.00 p.m.
Reds.......... 900,000
Hgn........... 19%
Whites........ 5,740

In the fresh blood the red cells varied greatly in size, and were pale in color. There were numerous microcytes, and few macrocytes. No normoblasts were seen.

March 29, 1907, 10.00 a.m.
Reds.......... 676,000
Hgn........... 15%
Whites........ 6,360

The pigmentation of the face had deepened perceptibly. The sclerotics were definitely jaundiced. In the fresh blood there was no rouleaux formation. There was marked poikilocytosis with many sausage- and pear-shaped cells. There was a moderate number of megalocytes. There was marked anisocytosis. There was a moderate number of microcytes. It was the exception to find well-formed red cells. There were occasional intermediates and normoblasts seen. The patient became unconscious the last night, and was never roused. There was marked air hunger. Death occurred at 5.30 p.m.

(See Chart, Fig. 48.)

Case B. Bell and Osler.

Pernicious Anemia; Transfusion; Death in about Forty-eight Hours; Autopsy

The patient was a male, forty-seven years of age, with the ordinary symptoms of pernicious anemia. The account of the examination of the blood is as follows: "The blood examined during life was very thin, watery, and of pale claret color. It presented the following characteristics: Colorless corpuscles appear perfectly natural in structure and size, and are not numerically increased. No large granular ones, such as described by Litten, could be found. Two forms of colored corpuscles—(*a*) ordinary forms, which are paler than natural, flattened out, less biconcave, and are very irregu-

lar in outline, some ovoid, others with sinuous borders, others again with pointed processes. (*b*) Small red corpuscles—microcytes—erroneously described by Eichorst as pathognomonic of this affection. They were numerous, 8 to 10 occurring in the field of No. 9 im. and oc. 3. The diameter ranged from $\frac{1}{5000}$ inch to $\frac{1}{9000}$ inch. They equaled, or even exceeded, in coloration the ordinary forms; some were crenated, and they frequently presented a pit or cuplike

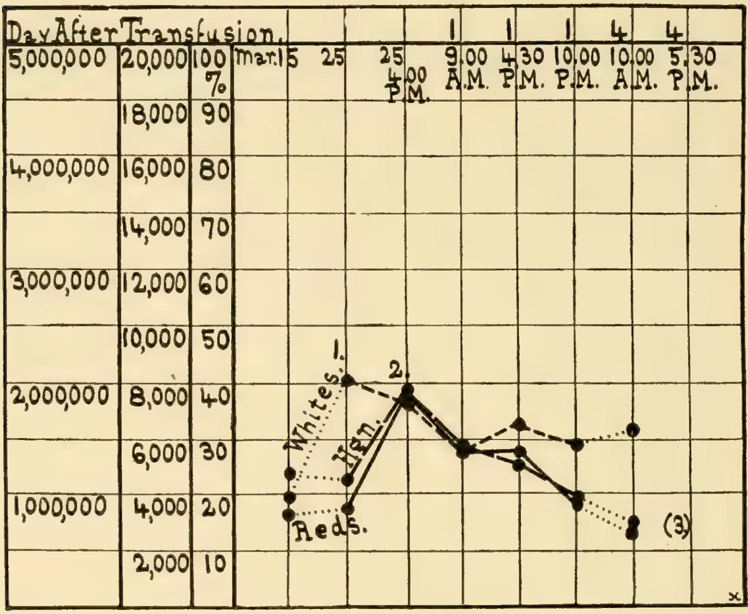


FIG. 48.—DR. STEPHEN H. WATT'S CASE OF PERNICIOUS ANEMIA. BLOOD CHART OF RECIPIENT. 1, 2. Before and after transfusion. 3. Death. Duration of transfusion, eighty minutes. Note rapid hemolysis after the transfusion.

depression on one side. In the repeated examinations of the blood, extending over three months, these forms increased but little numerically. Schultze's granular masses were not noticed. No appreciable difference could be detected in the histological appearance of the blood an hour after the transfusion."

At the transfusion six ounces of defibrinated human blood were injected into the patient's veins. The immediate effect of the new blood was to cause an increased fullness of the superficial veins, a pinker color of the lips, and increased moisture of the skin. Before

the transfusion the pulse was 102, and the temperature 99.1°. Half an hour after the transfusion the patient complained of feeling chilly, and the temperature began to rise. By the end of an hour there were marked rigors, the pulse was 120, and the temperature 102°. Three and one half hours after the transfusion the temperature reached the maximum of 104.1°. The night was well passed, and the next morning he said that he felt stronger and that his mind was clearer. The temperature continued to fall, but the next day it began to rise again, and death occurred about forty-eight hours after the operation.

The autopsy showed a marked general pallor of the tissues. A pint of bloody serum was found in one pleural cavity, and half a pint in the other. The lungs showed an excess of serosity. The spleen was slightly enlarged, and bound to the diaphragm, stomach, and colon by numerous adhesions. The liver showed a few ecchymoses in the capsule, and its substance was much softened in parts.

Case C. Kahler.

Pernicious Anemia; Transfusion; Death at the End of Eight Days; Autopsy

The patient was a woman, twenty-nine years of age, who was suffering from a rapidly progressing pernicious anemia, with hemorrhages into the skin of the trunk and extremities, and the eyes. The first blood examination showed 744,000 red cells per cubic millimeter, a reduced hemoglobin, and marked poikilocytosis. Apparently no examination of a stained blood smear was made. A transfusion of 104 c.c. of defibrinated human blood was performed. Immediately before the transfusion the red cells were 389,050 per cubic millimeter. Immediately after they had risen to 589,000, and there was a reddening of the face, and general improvement. The urine passed at first contained nothing abnormal. That passed one and a half hours after the transfusion was dark red in color and contained a large amount of albumin. No red cells were found on microscopic examination, but casts and renal epithelium were found. A chill occurred, and later the temperature rose to a maximum of 40° C. By the end of the day the urine contained no more hemoglobin and albumin. By the next day the red cells had fallen to 264,554 (lower than they were before the transfusion), and there was a corresponding fall in the hemoglobin. On the sixth and seventh days after the transfusion there were severe nosebleeds, and on the eighth day death occurred.

From the autopsy the pathological diagnosis was pernicious anemia, chronic pulmonary edema, and fatty degeneration of the heart.

Case D. Brakenridge (I).

Pernicious Anemia; Transfusion on Four Separate Occasions; Death after some Months

The patient was a woman, thirty-four years of age, who suffered from pernicious anemia. Her red cells before the first transfusion were 1,160,000 per cubic millimeter, and the hemoglobin 24 per cent. "Tailed" red cells were present, and the red corpuscles were "extremely unhealthy looking and varied in size, many of them being smaller than normal." An old hemorrhage was observed in the retina of the left eye. Various remedies failed to check the progress of the disease, so that it was decided to transfuse. On July 5th, six ounces of human blood diluted with one third its bulk of 1 to 20 phosphate of soda solution were injected intravenously. A gain of 310,000 red cells per cubic millimeter was noted, followed at the end of five days by a fall almost to the original point. The microcytes disappeared, and were not observed again. The red cells became normal in appearance. On July 12th, 26th, and August 7th, three more transfusions were performed, with a rise in the red cells after all but the last, when too strong a solution of sodium phosphate was employed. She was discharged as almost well, and remained fairly well for some months. The anemia recurred, and she died some months later.

Case E. Brakenridge (II).

Pernicious Anemia; Transfusion; Apparent Recovery after the Lapse of Three and a Half Years

The patient was a woman, twenty-five years of age. Her red cells at one time fell as low as 640,000, her hemoglobin to 20 per cent, and her white cells were not increased in number. There was poikilocytosis, and microcytes and a "number of distinctly nucleated large red blood corpuscles" were present. There were also the usual symptoms of pernicious anemia. When the number of red cells was lowest, $5\frac{1}{3}$ ounces of human blood, diluted as before, were injected intravenously. After this there was a tolerably steady rise in the number of red cells. By the end of a week they had risen to 2,080,000, i. e., they had more than trebled in number. Before the patient left the hospital they had risen to 4,000,000 per cubic millimeter, and the hemoglobin to 75 per cent. "This remarkable rise

in the number of corpuscles and fall in the temperature has been accompanied by a corresponding improvement generally. The pulse has steadily improved in volume, tension, and rate. The cheeks, gums, conjunctivæ, and finger nails have gradually assumed a rosier tint. She has also gained in strength. Her cardiac and venous murmurs gradually disappeared, and she gained about thirteen pounds in weight. Mrs. M. left the hospital on January 8, 1889—three and a half years ago—and has remained quite well since that date."

Case F. Brakenridge (III).

Pernicious Anemia; Patient almost in Extremis; Transfusion; Death Twenty-four Hours Later

The patient was a woman, twenty-seven years of age. Her blood at first had 715,000 red cells per cubic millimeter. A week later they had fallen to 480,000. The hemoglobin was 26 per cent. The white cells were apparently normal. There were a number of microcytes and nucleated red cells, some of large size. It was evident that the patient was going to die, but two ounces of human blood, diluted as before, were injected intravenously. A gain of 100,000 red cells per cubic millimeter followed. Death occurred the next night. The postmortem examination showed the characteristic changes of pernicious anemia—a large excess of iron pigment in the liver, reddening of the bone marrow, intense pallor of all the organs, and lemon-yellow color of all the fat.

CONCLUSIONS

Pernicious anemia in an advanced stage is not favorably modified by transfusion. It has not been demonstrated that it is favorably modified when in an early stage.

CHAPTER XVIII

LEUKEMIA

(*Group II*)

CASE NO. II, 1 (6,599). ABSTRACT. CONSULTATION WITH DR. J. R. ARNEILL, DENVER, COL.

Myelogenous Leukemia; Failure of Treatment; Transfusion; Death Twenty-two Days after Transfusion

The patient was an American woman, forty-two years of age, who complained of having a lump in her side. Her mother and one aunt died of carcinoma. Ten other members of the immediate family were living and well. Up to the time of the illness for which the transfusion was performed she had been quite healthy. Her gums had always bled easily. Her menstruation was normal.

Two and a half years previously she had had pain in her left side in the axillary line near the costal border. Within a week she became short of breath on exertion, her skin became pale and muddy, and her spleen was found to be enlarged. Up to just before the transfusion she had lost twenty pounds. A year previously she had had pneumonia, followed by improvement in the pain in her side, and her shortness of breath, and by reduction in the size of the splenic swelling. At about the same time, she received forty X-ray treatments, with some shrinking of the spleen and general improvement, which ceased gradually as soon as they were stopped. Edema of the ankles, present at this time, was relieved by hot baths. Her physician, Dr. Arneill, made the diagnosis of myelogenous leukemia. Finding thorough medical treatment to be without lasting effect, he referred her to be transfused as a last resort. When first seen she had a red count of 2,864,000, hemoglobin of 65 per cent, and a white count of 210,200. Her blood platelets numbered 572,000 per cubic millimeter, the coagulation time was three minutes, the blood-pressure 112 mm., and the specific gravity of the blood 1.050.

The fresh blood showed the presence of many myelocytes with all degrees of granular protoplasm, while the red cells appeared to be normal.

The donor was not related to the recipient. The anastomosis was made between a radial artery of the donor and a median basilic vein of the recipient. The suture method was employed. The blood was allowed to flow across for forty-eight minutes. The donor was only temporarily inconvenienced by his loss of blood. Extended blood examinations were made (for the details see page 345). After the wound of the recipient was sewed up there was considerable oozing of blood, and a tight compress had to be applied at forty-eight and sixty hours afterwards. The coagulation time had risen at first to eight minutes and thirty seconds. On giving calcium chlorid it was reduced to six minutes and thirty seconds.

Immediately after the transfusion there was a marked improvement in the patient's appearance, in her circulation, and in her spirits. Her red count had risen from 2,864,000 to 3,632,000, the hemoglobin from 65 to 85 per cent, and the white cells from 210,000 to 238,000. The specific gravity had increased from 1.050 to 1.053. There was a slight febrile reaction, and a slight chill.

By the end of the second week the spleen was smaller, but this cannot necessarily be attributed to the transfusion, as variation in the size of the spleen from time to time is not at all unusual in the natural course of the disease. The increase in the number of red corpuscles was not sustained, nor was the general blood picture improved. The patient had had some cough since entering the hospital. Three days before her death this increased, and symptoms of bronchitis became more marked. There was some dullness over the upper right chest, and fine moist râles. Vocal fremitus was increased over an area the size of the palm of a hand, just under the clavicle. On the twentieth day after the transfusion she became cyanotic—her heart sounds assuming an embryonic rhythm, with a weakened pulmonic second sound. Death occurred on the twenty-second day.

The pathologic diagnosis made at the autopsy was as follows: Leukemia of the spleno-myelogenous type, with perisplenitis, and enlargement of the spleen, liver, and kidneys, perihepatitis, healed splenic infarcts, marked pulmonary edema, fatty degeneration of the myocardium, acute cardiac dilatation, chronic interstitial nephritis, fibro-myomata of the uterus with calcification, bilateral cystic ovaries, and slight hyperplasia of the lymph glands.

Comment.—In the light of later clinical experience and experimental research, it would have been desirable to have bled the patient freely before transfusing in order to substitute as much new blood as possible for the leukemic blood. Both Dr. Arneill and the author took the view

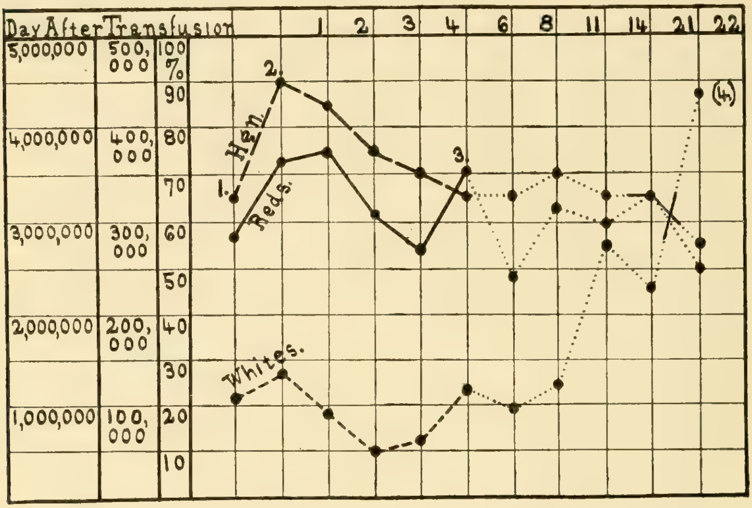


FIG. 49.—CASE NO. II, 1, (6599). BLOOD CHART OF RECIPIENT. MYELOGENOUS LEUKEMIA. 1, 2. Day before, and just after transfusion. 3. Blood lost from oozing from wound. 4. Death. Duration of transfusion, forty-eight minutes. Note.—It should be observed that the coördinates on this chart express the white corpuscles in *hundreds-of-thousands* instead of in thousands.

that the transfusion was purely a tentative measure, used as a last resort after all the other forms of treatment employed had failed. It would be interesting to observe what would happen in such a case if transfusion could be employed much earlier in the course of the disease. As it was, in this case it did not seem that the course was much modified, and certainly not at all in preventing the fatal termination.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count	Platelets	Coag. Time	Blood-Pressure	Sp. Gr.
Before.[1]	2,864,000	65%	210,200	572,000	3′ 0″	112 mm.	1.050
After.[2]	3,632,000	90%	238,000	363,200	4′ 35″	107 mm.	1.053
1st day.	3,704,000	85%	192,600	119,500	9′ 10″	112 mm.	1.051
2d day.	3,096,000	75%	146,000	206,000	8′ 20″	115 mm.	1.050
3d day.	2,680,000	70%	160,400	134,000	8′ 30″	118 mm.	1.049
4th day.	3,472,000	65%	215,000	290,000	6′ 40″	115 mm.	1.049
6th day.	2,376,000	65%	195,000	339,000	3′ 0″[3]	115 mm.	1.047
8th day.	3,152,000	70%	220,000	450,000	3′ 10″	....	1.053
11th day.	2,950,000	65%	375,000	365,000	4′ 50″	....	1.053
14th day.	3,288,000	65%	328,800	548,000	3′ 15″	112 mm.	1.049
21st day.	2,480,000	55%	536,000	206,600	3′ 15″	110 mm.	1.052

[1] The day before the transfusion. [2] Just after the transfusion.

[3] Calcium chlorid was given at this time to increase the coagulability.

(See Chart, Fig. 49.)

The Blood-Pressure, Pulse Rate, and Hemoglobin Changes During the Transfusion.

Time	Pulse	Blood-Pressure	Hemoglobin	Remarks
10.30 A.M.	72	115 mm.	....	Began to transfuse.
10.35 A.M.	72	110 mm.	....	
10.40 A.M.	72	105 mm.	65%	
10.45 A.M.	80	115 mm.	....	The patient vomited.
10.50 A.M.	72	110 mm.	....	
10.55 A.M.	72	102 mm.	....	
11.00 A.M.	72	102 mm.	65%	
11.05 A.M.	84	120 mm.	....	The patient vomited.
11.10 A.M.	60	102 mm.	....	
11.30 A.M.	76	105 mm.	75%	
11.40 A.M.	80	110 mm.	75%	
11.55 A.M.	80	105 mm.	80%	
12.01 A.M.	..	....	....	The transfusion was stopped. The flow lasted a total of forty-eight minutes, but was interrupted as occasion demanded.

The Donor

Time	Red Count	Hemoglobin	White Count	Platelets	Coag. Time	Blood-Pressure	Sp. Gr.
Before.	5,912,000	100%+	10,000	....	7′ 0″	130 mm.	1.058
After.	5,360,000	95%	13,600	412,000	5′ 0″	115 mm.	1.055
1st day.	5,320,000	100%	5,600	241,818	8′ 20″	128 mm.	1.056
2d day.	5,688,000	95%+	12,800	146,000	8′ 0″	120 mm.	1.059
3d day.	5,504,000	100%+	8,000	458,000	4′ 0″	135 mm.	1.056

(See Chart, Fig. 8, p. 91.)

SUMMARY

CASE No. II, 1 (6,599).

Transfused.—For myelogenous leukemia.

Immediate Result.—Marked temporary improvement.

Other Treatment.—None.

Late Result.—Death twenty-two days after transfusion.

CASES FROM OTHER SOURCES

CASE A. ANDREW AND CALLENDER.

Leukemia; Transfusion on Two Different Occasions of Small Amounts of Blood; Temporary Improvement Only; Late Results Not Known

The patient was a girl, seven years of age, who was afflicted with a condition diagnosed as leukemia. She had enlarged glands in the neck, an enlarged spleen, which extended some distance below the left hypochondrium, and an unusual number of leucocytes in her blood. She was anemic, her respirations were 20 per minute, and her pulse was 189, of fair volume and regular. Under quinine no improvement resulted. After a few weeks of treatment she began to have diarrhea, and her previously normal temperature rose to 102° F. One ounce of defibrinated human blood was injected intravenously by means of a funnel, tube, and syringe. On the morning of the transfusion the temperature was as above stated. By evening it had fallen to 99°, and the next day it was normal. To quote the words of the writers: "The proceeding was followed by marked improvement for a time; the temperature remained normal, the diarrhea ceased, the general condition of the patient improved with returning appetite, the glandular swelling, the enlarged spleen, and the leukemic condition of the blood all decreased. The only unfavorable circumstance was that a troublesome sore made its appearance on the thumb of the side on which the injection had been made, and that the operation wound was long in healing, slight suppuration taking place in it." Five weeks later, at a second transfusion, 3 ounces of defibrinated human blood were injected with success as before. "During the first few days there was considerable edema over the enlarged glands, but when this subsided, the glands were found to be smaller and softer. Unfortunately, the benefit was again only temporary; the child's general condition fell

off, the sore on the thumb proved very intractable, and . . . her friends were unwilling to consent to a third operation. . . . I have not been able to learn her subsequent history. . . ."

Case B. Mosler.

Leukemia; Preliminary Bleeding; Transfusion; General Condition Improved; Diminution of Number of White Cells Noted at End of Two Weeks; Late Results Not Known.

The patient was a male, thirty-four years of age, who was suffering from a condition diagnosed as leukemia. He complained of pain in his left side, shortness of breath, and weakness in his legs. He was very anemic, had diarrhea, the spleen and liver were enlarged, and the number of white corpuscles in the blood was steadily increasing. At one time the ratio between white and red corpuscles was 1 : 18. Tonic treatment did not relieve the patient, and after removing 140 c.c. of his blood, 180 c.c. of defibrinated human blood were injected intravenously. An hour after he had a chill, which lasted one and a half hours. His general condition was considerably improved. He became constipated. The number of white corpuscles was found to be diminished when the blood was examined about two weeks after the transfusion, but no later or more definite history is given.

Case C. Gallaher.

"Leucocythemia"; Steady Failure of Patient in Spite of Treatment; Transfusion; Death Thirteen Hours Later

The patient was a male, sixty-three years of age. For forty years he had had a chronic affection of the spleen. He complained of uneasiness in the epigastrium, and loss of weight, appetite, and strength. The spleen was much enlarged, extending half an inch below the umbilicus. His blood showed one white to every fifteen red corpuscles. Later in the course of the disease he had diarrhea, and lost still more weight. As all the forms of treatment which were employed did not relieve him, it was decided to transfuse. Immediately before the transfusion his radial pulse could scarcely be felt at the wrist. Nine ounces of venous blood taken from the patient's son were defibrinated and strained, and then injected intravenously. No unpleasant symptoms developed during the process. In a few minutes an improvement in the pulse and temperature was quite perceptible, but in less than half an hour the effects passed away. The next morning the patient complained of pain in his back.

He passed no urine. Death occurred at 10 A.M., thirteen hours after the transfusion.

CONCLUSIONS

Leukemia in an advanced stage is not favorably modified by transfusion. It has not been demonstrated that it is favorably modified when in an early stage.

CHAPTER XIX

SARCOMA

(*Group III*)

Case No. III, 1 (7,173). Abstract. Consultation with Dr. W. J. Frick, Kansas City, Mo.

Perithelial Angiosarcoma of the Neck; Three Previous Operations, with Recurrence after Each; Complete Block Dissection of Neck, with Removal of Left Tonsil and Posterior Edge of Tongue; First Transfusion at End of Four Days; Excellent Recovery; X-ray Treatments Begun; Second Transfusion One Month Later; Excellent Recovery; Continued X-ray Treatments; No Recurrence at End of Three Months.

The patient was an American, thirty-nine years of age, who complained of "cancer" of the neck. His family history was entirely negative, and his personal history had no bearing on the disease under discussion.

About eighteen months previously he had first noticed a small lump the size of a hazel nut in the left side of his neck. A year later this had grown to the size of a hen's egg, and was removed by Dr. Frick. Up to that time the patient had felt very well, and had had no pain or discomfort. A little later a small gland containing pus was removed from behind the ear, and another hard one at the lower end of the incision. Five months after the first operation a third operation was performed, and a lump removed which was pressing on the tonsil.

The physical examination showed the left tonsil to be slightly enlarged, red, with the surface apparently raw, and sore to the touch. No enlarged glands could be palpated on either side of the neck. The tissue about the scar was indurated. Otherwise the physical examination was negative.

At the operation the patient was etherized through nasal tubes in the customary way in operations of this character, and the head

of the table was elevated. The lower extremities were incased in a rubber pneumatic suit. The carotid artery was clamped temporarily, and a thorough block dissection made of the scar and surrounding regions, with excision of the tonsil and a portion of the edge of the tongue. The patient's condition after the operation was good. On the following day X-ray treatments were begun.

First Transfusion.—On the fourth day after the operation the patient was transfused for twenty-nine minutes from a brother. One of the donor's radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The transfusion was without particular incident. The patient's face became somewhat flushed. There was no preliminary bleeding (there had been a free discharge of serum from the tissues, and a certain amount of blood was lost at the operation, although very little, considering its nature). The right heart did not dilate. The patient complained of no discomfort, but said that his head felt "full." His red count rose from 4,500,000 to 5,080,000, his hemoglobin from 90 to 95 per cent, and his white count from 11,900 to 13,800. By the next day the red count was reduced to 4,832,000, and the hemoglobin to 90 per cent.

One month later the hemolysis had lessened very materially. The patient's general condition was good. The wound was clean, and healing slowly but steadily. The X-ray treatments had been continued during this time. The red count had risen to 5,120,000, the hemoglobin was 90 per cent, and the white count was 10,600. The left side of the tongue posteriorly felt thickened, and troubled the patient by getting between his teeth. There was no sign of recurrence. The situation as a whole was so favorable that it was decided to transfuse again.

Second Transfusion.—Another brother served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for thirty minutes.

The patient said that his arm felt cold and numb, but that after a few minutes the numbness disappeared, and it became warm. His head soon felt full again, but there was no acute cardiac dilatation, although a preliminary bleeding was not done. The immediate strong stimulation was noted as at the first transfusion. Immediately after the flow stopped there was a sudden chill, with rapid rise of temperature to 101° F. It soon fell to normal again.

The next day the patient was in excellent condition. In a short time there was less pain and tenderness in the maxillary joint, the

wound continued to heal slowly, the voice was still husky, and the right side of the face was somewhat swollen. Three days after the second transfusion the patient was sent home. X-ray treatments were begun again. Up to the present time, three months after the second transfusion, there has been no sign of recurrence of the growth. The pathologist reported that it was a perithelial angiosarcoma.

Comment.—In case there should be no recurrence of the growth at a future date, the fact must be remembered that transfusion was but one of three methods of attack, the other two being the thorough operation and the long use of the X-rays. As far as is known, the donors had no acquired immunity to sarcoma, but they might have possessed a certain amount of natural immunity.

Case No. III, 2 (7,124). Abstract. Consultation with Dr. M. J. Hawkins, Brunswick, Ohio.

Inoperable Sarcoma of Neck; Use of Coley's Toxins for Three Months; Shrinkage of Tumor from One Half to One Third; Stationary Condition for Some Time; Active Growth at End of Nine Months; Preliminary Bleeding; Transfusion from Two Donors; Death Eight Months after Transfusion.

The patient was an American, thirty-six years of age, who complained of having a lump in his neck. His father died of a cardiac lesion, and a sister of tuberculosis. There was no history of hemophilia or neoplasm. Other members of the family were well. His personal history was negative.

Five months previously the patient had noticed a lump in the left side of his neck just above the clavicle. The lump was the size of a hickory nut, and the skin over it was reddened. Two months previously he had noticed that red streaks were beginning to radiate from the mass down over the chest, and that the size had increased. There was no pain, and the mass was always hard.

The general physical examination was negative. In the left posterior triangle of the neck there was a hard oval mass 6 cm. in greatest diameter. It was hard and firmly adherent to the underlying structures and the skin. It was not adherent to the clavicle, although pressing on it. The diagnosis of sarcoma was made, and was confirmed by microscopical examination. It was of the large

round-cell variety. Its position, attachments, and extent of development rendered it inoperable.

Under X-ray treatment and the use of Coley's toxins for a period of three months the patient gained 9 pounds, and the tumor mass shrank between one third and one half and became softer. Then the patient was lost sight of for nine months. At the end of that time he had had soreness over the upper part of his sternum for six weeks, induration of the lower part of the neck, and, one week before entrance, rapid swelling over the upper part of the sternum, with fluctuation. The whole mass was densely adherent to the surrounding structures. He had had cough for six weeks, with copious muco-purulent expectoration, and thought he had lost from 10 to 15 pounds in weight. As a last resort it was decided to try transfusion.

Two donors were used who were not related to the patient. They were both young men in good condition. The first donor weighed 169 pounds and lost $1\frac{1}{2}$ pounds. The second donor weighed 173 pounds and lost $3\frac{15}{16}$ pounds. The first suffered no inconvenience at all. The second was about to faint when disconnected from the recipient, but revived when cold water was dashed on his abdomen. One hour after his return to the ward, a nurse had him walk upstairs to be weighed. On his return he collapsed—was pulseless at the wrist, nauseated, faint, and perspiring. His head was lowered, his extremities bandaged, and he was given a small dose of strychnin. The symptoms gradually cleared up, so that by the next morning he was able to return to his home without difficulty. Both donors were connected to the recipient by cannula anastomosis of a radial artery to a superficial vein of the upper arm in the usual way.

Before the transfusion was begun, the patient's lower extremities were placed in a rubber pneumatic suit. He was then gradually bled 1,400 c.c. As this was done, the suit was slowly inflated, and he was lowered more and more into the head-down position to prevent cerebral and cardiac anemia during the bleeding. The blood from the first donor was allowed to flow across for forty minutes, and from the second donor for fifty-six minutes. The day before the transfusion the red count was 4,480,000, the hemoglobin 80 per cent, and the white count 8,800. Immediately after the red count was 4,344,000, the hemoglobin 65 per cent, and the white count 7,000. The transfusion was followed by a chill and a rise of temperature to 104.6° F.

Later there was a gain in weight. During the first two months following the transfusion the tumor gradually decreased in size. Later

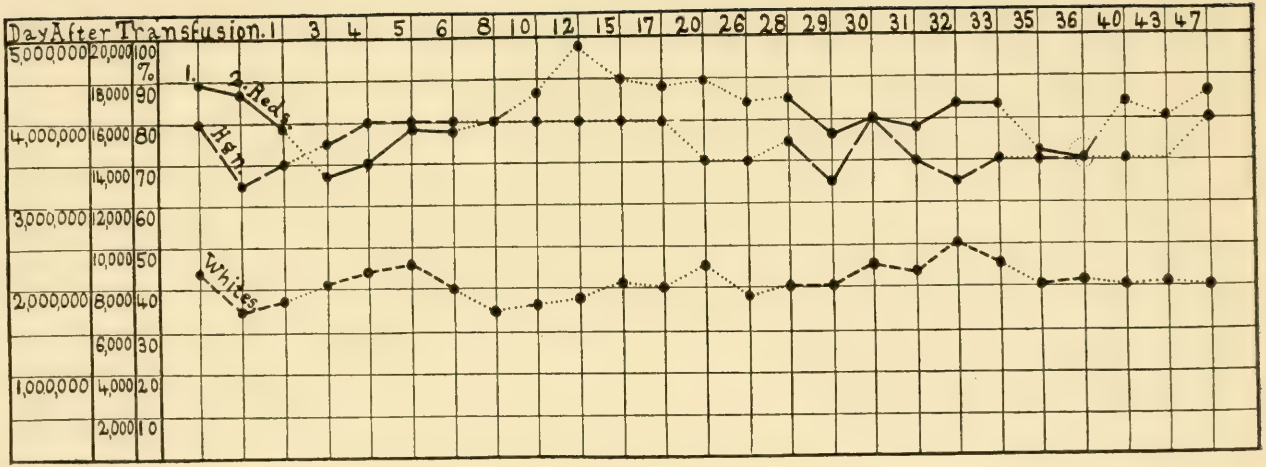


FIG. 50.—CASE NO. III, 2 (7124). BLOOD CHART OF RECIPIENT. SARCOMA OF NECK.
1, 2. Just before, and just after transfusion. Duration of transfusion, forty minutes.

still there was a gradual increase in the growth. A second transfusion was proposed, but was not carried out. Two months after the transfusion the patient was discharged. Death occurred six months later.

Comment.—The final outcome was not altered in spite of the temporary encouragement.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Day before.	4,480,000	80%	8,800
Just after.	4,344,000	65%	7,000
1st day.	3,936,000	70%	7,400
3d day.	3,360,000	75%	8,200
4th day.	3,520,000	80%	8,800
5th day.	3,936,000	80%	9,000
6th day.	3,900,000	80%	8,000
8th day.	4,000,000	75%	7,000
10th day.	4,320,000	80%	7,400
12th day.	4,900,000	80%	7,500
15th day.	4,500,000	80%	8,200
17th day.	4,416,000	80%	8,000
20th day.	4,480,000	70%	9,000
26th day.	4,200,000	70%	7,500
28th day.	4,256,000	75%	8,000
29th day.	3,800,000	65%	8,000
30th day.	4,000,000	80%	9,000
31st day.	3,900,000	70%	8,600
32d day.	4,160,000	65%	10,000
33d day.	4,160,000	70%	9,000
35th day.	3,600,000	70%	8,000
36th day.	3,520,000	70%	8,200
40th day.	4,200,000	70%	8,000
43d day.	4,000,000	70%	8,200
47th day.	4,300,000	80%	8,000

(See Chart, Fig. 50.)

CASE NO. III, 3 (6,853). ABSTRACT. CONSULTATION WITH DR. J. B. MCGEE.

Sarcoma of the Upper Jaw, Involving the Ramus of the Lower Jaw; Excision; Transfusion; Recovery; X-ray Treatment; No Return of Growth in Twelve Months.

The patient was a German woman, sixty years of age, who had a negative family history, and whose complaint was that she had a

lump in her lower jaw. Seven months previously she had had a new lower plate made. The plate was a little too large, and caused irritation by rubbing against the cheek. Two months later a nodule in the cheek suppurated, and broke one month before she entered the hospital. The nodule was always hard. She had had dull pain from the beginning and had lost weight.

At the physical examination no glandular enlargement or other evidence of metastasis was found. There was a varicose ulcer of the left lower third of the shin and the outer aspect of the instep. The left cheek was swollen over an area 7 cm. in diameter to a height of 1 cm. The swelling was hard and firmly attached to the lower jaw. The overlying skin was movable. On the inside of the cheek, extending over on the alveolar edge, was a large excavated ulcer, with a suppurating center 1 cm. deep and 2 cm. in diameter. The edges of the ulcer were curled and raised.

The pharynx was packed with gauze around rubber tubes passed through the nostrils, through which the ether was given. The carotid was temporarily clamped, and the lower jaw resected with the adherent tumor. The wound was left open for later X-ray treatment. The pathologist reported the growth to be a mixed round- and spindle-celled sarcoma. As the size of the tumor, its location, and especially its histologic variety rendered the chances as to the outcome extremely grave, transfusion was performed.

A son of the patient served as donor. One of his radial arteries was anastomosed to a venous branch near the elbow of the patient by the cannula method. The blood was allowed to flow across for twenty minutes.

The patient immediately showed marked improvement in every way. The red count rose from 4,384,000 to 5,240,000 in three days, the hemoglobin immediately rose from 80 to 90 per cent, and later to 100 per cent, and the white count was unaffected. She gained in weight and strength, surpassing to a very marked degree her condition before the operation. There was no sign of recurrence in twelve months, and at that time her health was excellent. Her blood serum showed no hemolytic action.

Comment.—The prognosis from the purely surgical standpoint was certainly most grave. As yet it cannot be determined whether transfusion favorably influenced this case or not.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Day before.	4,384,000	80%	7,000
Immediately after.	4,546,000	90%	8,040
1st day.	4,580,000	90%	7,000
3d day.	5,240,000	95%	8,400
6th day.	5,120,000	90%	8,000
7th day.	5,100,000	90%	8,040
9th day.	5,040,000	90%	7,000
11th day.	5,120,000	90%	7,040
12th day.	5,280,000	100%	7,000
13th day.	5,200,000	100%	7,080
15th day.	5,280,000	100%	6,800

(See Chart, Fig. 51.)

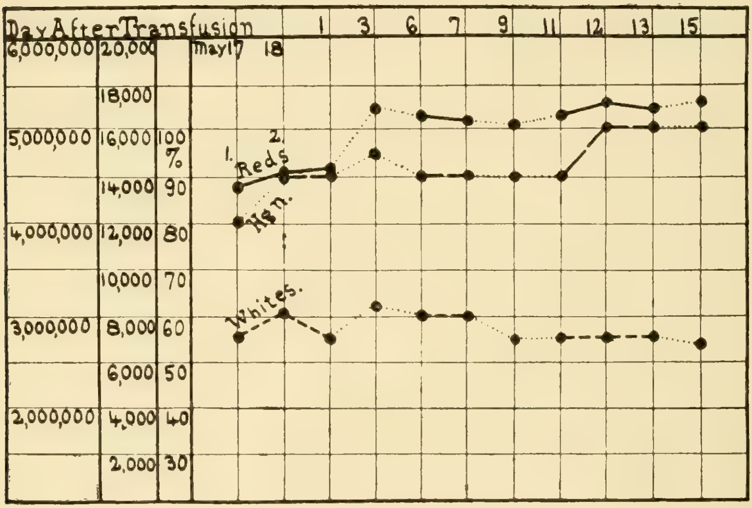


FIG. 51.—CASE NO. III, 3, (6853). BLOOD CHART OF RECIPIENT. SARCOMA OF LOWER JAW. 1, 2. Day before, and just after transfusion. Duration of transfusion, twenty minutes.

The Recipient During the Transfusion.

Time	Blood-Pressure	Pulse	Respiration
1.40 P.M.	140 mm.	112	16
1.46 P.M.	140 mm.	120	20
1.49 P.M.	140 mm.	120	16
1.55 P.M.	150 mm.	118	20
2.00 P.M.	160 mm.	118	20

The Donor

Time	Red Count	Hemoglobin	White Count
Day before.	5,120,000	100%	8,040
Immediately after.	4,980,000	95%	10,800
7 hours after.	4,890,000	90%	20,400
3d day.	5,520,000	100%	11,200
7th day.	5,580,000	100%	9,000

(See Chart, Fig. 9, p. 93.)

Case No. III, 4 (7,052). Abstract. Consultation with Dr. R. B. Gamble, Meadville, Pa.

Sarcoma of the Testicle, with Extensive Metastases into the Abdomen via the Retroperitoneal Lymph Glands; Exploratory Laparotomy; Recognition of Hopelessness of Case from Operative Standpoint; Transfusion without Preliminary Bleeding; Death of Patient at End of Three Months.

The patient was an American, twenty-four years of age, who complained of having an enlarged left testicle. His family history contained no record of neoplasm, tuberculosis, or hemophilia. He had had gonorrhea three times, but denied having had syphilis. Otherwise his personal history was negative.

About one year previously he had noticed that his left testicle was increasing in size. During the month before he came to the hospital he thought it had been growing more rapidly. It was never painful, but he had had a dragging sensation when much on his feet. For three weeks previously he had noticed that the left side of his abdomen was increasing in size, and that a mass could be felt there. He had had a dull aching pain in this area during a good part of the time, and also in his left lumbar region. He had had no fever. He had lost 15 pounds in weight.

The physical examination showed that the splenic area was enlarged. The edge of the spleen could not be felt on account of the presence of the mass in the abdomen interfering. In the region of the umbilicus, but mostly to the left of the median line, there was a hard, slightly movable, not tender, dome-shaped, projecting mass about 14 × 18 cm. in size. The right testicle was smaller than normal. The left part of the scrotum contained a 11 × 11 cm. hard tumor involving the left testicle and epididymis.

At the operation the abdominal cavity was opened by a 6 cm.

median incision. A large and rather soft mass was found arising from the retroperitoneal glands. The intestines, stomach, omentum, etc., were densely adherent to it, and immense blood-vessels ran over its surface. It was decided that it would be useless to try to remove it. A small gland was excised, and in doing so a vein was opened, which bled profusely. This was clamped and tied off with linen thread. The abdomen was then closed. The mass in the scrotum was not touched. Transfusion seemed to offer the only hope, as the tumor was a sarcoma which originated in the testicle and metastasized to the retroperitoneal lymph glands. Hemolysis experiments

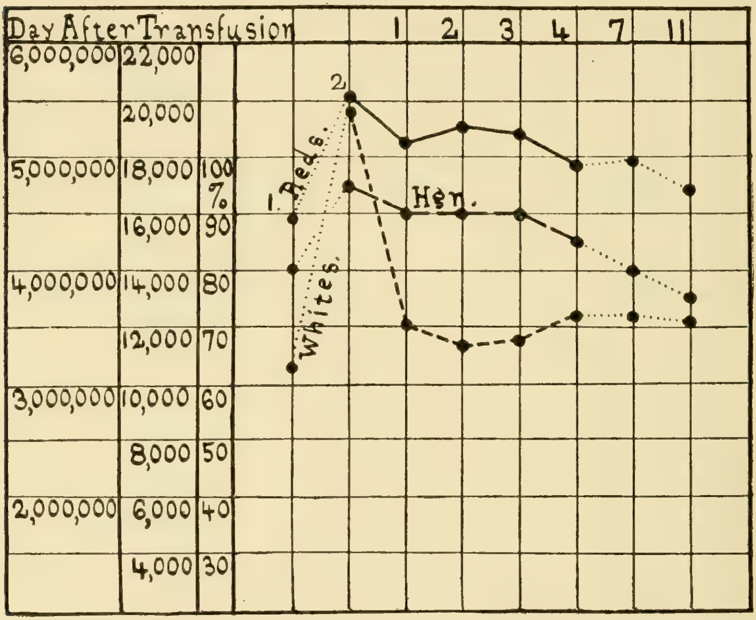


FIG. 52.—CASE NO. III, 4 (7052). BLOOD CHART OF RECIPIENT. SARCOMA OF TESTICLE WITH METASTASES IN ABDOMEN. 1, 2. Three days before, and just after transfusion.

made on the day before transfusion showed that the serum of the donor did not hemolyze the red corpuscles of the recipient, but that the serum of the recipient did hemolyze the red corpuscles of the donor.

The donor was a young man who was not related to the patient. One of his radial arteries was anastomosed to a median basilic vein

of the patient by the cannula method. The blood was allowed to flow across for twenty-one minutes.

The color of the patient improved noticeably during the transfusion, but after it was over he was somewhat cyanotic, and his right heart was found to have dilated out 1 cm. from the border of the sternum. The dilatation was of short duration, and no harm resulted from it. The patient's red cells rose from 4,456,000 to 5,520,000, the hemoglobin from 80 to 95 per cent, and the white cells from 10,500 to 19,800. The blood-pressure rose from 85 to 125 mm.

The immediate recovery was uneventful. No regression of the tumor was noted. Growth continued. The patient died three months after the transfusion.

Comment.—The transfusion was done as a last resort. The new blood exerted no apparent influence upon the tumor.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
3d day before transfusion.	4,456,000	80%	10,500
Immediately after transfusion.	5,520,000	95%	19,800
1st day.	5,120,000	90%	12,000
2d day.	5,262,000	90%	11,400
3d day.	5,200,000	90%	11,500
4th day.	4,904,000	85%	12,400
7th day.	4,961,000	80%	12,390
11th day.	4,716,000	75%	12,200

(See Chart, Fig. 52.)

CASE NO. III, 5 (7,371). ABSTRACT. CONSULTATION WITH DR. W. O. OSBORN.

Sarcoma of the Forearm; Amputation; Transfusion Nine Days Later; Death from Cerebral Metastasis Four Months Later.

The patient was a Canadian woman, fifty-nine years of age, who complained of having a tumor in her arm. Her family had no history of neoplasm, tuberculosis, or hemophilia. She had never been ill.

About a year previously she had strained her right arm in trying to pull down a window. Two months later she noticed soreness and

a small lump on the ulnar side of the forearm just above the wrist. This gave her little trouble until three months later. Then the lump began to enlarge a little, and her arm felt stiff. It was not until eight months after the strain that she consulted her physician. He opened the growth down to the bone. After that she began to have a great deal of pain, the wound did not heal, the growth increased in size, and she lost flesh and strength. During the two weeks before entrance the wound had bled much of the time. The hemorrhage during the change of dressings was so profuse as to necessitate the employment of a tourniquet.

The physical examination showed the patient to be cachectic, anemic, bedridden, and *in extremis*. There was no glandular enlargement. The cardiac dullness extended to the right of the sternum. At the apex the second sound was reduplicated, and accompanied by a soft systolic murmur. The second pulmonic sound was accentuated. On the ulnar side of the right forearm, just above the wrist, was a large mass, involving the entire cross dimension. It was red; the overlying skin was broken and ulcerating; it was tender, and only slightly movable. On moving hand or arm there was much pain. The diagnosis was made of sarcoma, and later confirmed by microscopical examination.

Under nitrous-oxid anesthesia the arm was amputated just above the elbow. The patient endured the operation well.

On the ninth day after the operation the patient was transfused from a daughter. The preliminary hemolysis tests were as follows:

1. Serum of donor + red cells of donor = no autolysis.
2. Serum of patient + red cells of patient = slight autolysis.
3. Serum of patient + red cells of donor (i. e., normal cells) = hemolysis.
4. Serum of donor + red cells of patient = no hemolysis.

On account of the fourth reaction being somewhat doubtful, it was decided to proceed with the transfusion, but with extreme care. If reverse hemolysis had been clearly shown, transfusion would not have been attempted.

A radial artery of the donor was anastomosed to a median basilic vein of the patient by the cannula method. The blood was allowed to flow across for twenty-six minutes. The patient was bled freely before the flow began.

After the transfusion the patient's pulse rate had fallen only 2 beats per minute, while the respiration came down from 30 to

24. The blood-pressure had risen from 108 to 126 mm. Her color was better, she had no cyanosis, no acute dilatation of the heart, and felt better in every way. There was no evidence of hemolysis from the transfusion. The change of blood was not as great as was desired.

The convalescence of the operation was uninterrupted. The patient was discharged eighteen days after the operation. At the time of her discharge there was a metastasis in her brain from which death occurred four months later.

Comment.—The patient's condition was so critical that it was by no means certain that an attempt should even have been made to send her to the hospital. While the transfusion markedly improved her general condition, it did not check the growth of the sarcoma.

CASE NO. III, 6 (7,370). ABSTRACT. CONSULTATION WITH DR. H. C. AURAND, BELLEVUE, OHIO.

Sarcoma of the Thigh; Preliminary and Final Operations, with Complete Removal of the Tumor at the Latter; Two Transfusions from the Same Donor, with Twelve Days' Interval Between; Immediate Result—Recovery; Late Results—To be Determined.

The patient was an American, twenty-six years of age, who complained of having a growth in his left thigh. His mother died of cancer of the stomach when fifty-three years old. Otherwise his family had no history of neoplasm, tuberculosis, or hemophilia. His own health had always been good.

About six months previously he had noticed a lump the size of a hen's egg in his left thigh on the posterior side. It was movable, hard, and had gradually increased in size. Occasionally there was a little dull aching pain. As far as he knew he had never injured his leg. He had not lost any weight.

The general physical examination was negative, beyond showing that the patient was in excellent general condition. On the posterior surface of his left thigh, just above the popliteal space, there was an incision about 4 cm. long, through which a piece of the tumor had previously been removed for microscopical examination. About this incision there was marked swelling and induration of the lower third of the thigh, so that it was difficult to palpate a definite mass.

The calf of the leg was somewhat swollen. To make the diagnosis certain the tumor was incised.

Under nitrous-oxid anesthesia a 6 cm. incision was carried deep down into the muscles. Rather soft pieces of broken-down tumor were removed with the finger. The cavity was thoroughly curetted and packed with iodoform gauze. Large, hot bichlorid-of-mercury dressings were applied. One week later a second operation was done on a more extensive scale. The dissection was carried round the tumor on all sides. It was then found not to have invaded the bone, although it extended down to the periosteum. It was circumscribed so that it could be dissected out *en masse*. In doing this it was necessary to sever the external popliteal nerve just after it left the sciatic, and to sever one of the inner hamstring tendons. The patient stood the operation well.

First Transfusion.—Eleven days after the operation the first transfusion was performed. Three days previous to the transfusion the hemolysis tests showed hemolysis. The donor was a strong, healthy farmer, who was not related to the patient. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The flow of blood was very strong, so that the transfusion was allowed to continue only eight minutes. The donor became slightly pale by the time it was over, but suffered no inconvenience.

Before the transfusion the patient was bled freely. By the time it was over his face was almost as bright a shade of red as if he had scarlet fever. He complained of feeling "queer," and said he felt as if his head and body were going to burst. His right heart did not dilate. The stream was partially shut off by compression of the artery with the fingers, and the patient was put in the head-up position. After the transfusion he was given small doses of digitalis. The recovery was entirely uneventful.

Second Transfusion.—Twelve days after the first transfusion (twenty-three days after the operation) a second transfusion was performed in the same way from the same donor. As before, the blood was allowed to flow across under strong pressure for eight minutes. The patient was affected just as before, except that toward the end of the flow he became cyanotic. He had no acute cardiac dilatation. There was no evidence of hemolysis. The wound in the leg was much cleaner, and healing well, when he was discharged from the hospital, nine days after the second transfusion.

Eight months after the second transfusion the patient was well,

and his blood showed no hemolytic action. At a later date a metastasis into the thorax had developed.

Comment.—Transfusion did not prevent subsequent metastasis formation.

SUMMARY

CASE NO. III, 1 (7,173).

Transfused.—On two separate occasions, one month apart, for perithelial angiosarcoma of neck.

Immediate Results.—Improvement following each transfusion.

Other Treatment.—Complete block dissection of neck, removal of tonsil and portion of tongue before first transfusion, X-ray treatments between the transfusions and after the second one.

Late Result.—No sign of recurrence at end of three months.

CASE NO. III, 2 (7,124).

Transfused.—For inoperable sarcoma of neck.

Immediate Result.—Regression for about two months.

Other Treatment.—Coley's toxins and X-ray treatments were given before the transfusion. Otherwise none.

Late Result.—Death from sarcoma eight months after transfusion.

CASE NO. III, 3 (6,853).

Transfused.—For sarcoma of lower jaw.

Immediate Result.—Beginning marked improvement in every way.

Other Treatment.—Resection of lower jaw; X-rays.

Late Result.—No sign of recurrence at end of twelve months. Patient in excellent condition.

Case No. III, 4 (7,052).

Transfused.—For inoperable sarcoma of retroperitoneal lymph glands metastatic from testicle.

Immediate Result.—Inconsequential.

Other Treatment.—Exploratory laparotomy.

Late Result.—Death from sarcoma at end of three months.

Case No. III, 5 (7,371).

Transfused.—For sarcoma of the forearm.

Immediate Result.—General improvement.

Other Treatment.—Amputation.

Late Result.—Death from sarcoma at end of four months.

Case No. III, 6 (7,370).

Transfused.—For sarcoma of thigh on two separate occasions with twelve days' interval.

Immediate Results.—Good recoveries.

Other Treatment.—Excision of tumor (before first transfusion), preliminary bleeding.

Late Result.—Patient well, with no hemolytic action at end of eight months.

CONCLUSIONS

Interesting facts are being learned from transfusion for sarcoma. Whether they will prove to be of clinical value is undetermined. At the present time the most that can be said is that but slight encouragement is offered.

CHAPTER XX

CARCINOMA

(*Group IV*)

Case No. IV, 1 (6,850). Abstract. Consultation with Dr. C. W. Thomas, Warren, Ohio.

Adenocarcinoma of the Axilla and Scapula (Metastatic from the Breast); Resection of Portion of Scapula; Thorough Excision of Tumor, including Three Quarters of an Inch of Axillary Artery; Restoration of Axillary Artery by End-to-end Anastomosis by Carrel's Method; Transfusion, with Hope of Influencing any Unremoved Growth; Recovery; Recurrence of Cancer in a Few Months; Persistence of Circulation in Axillary Artery at End of Eleven Months.

The patient was an American woman, fifty years of age. Her family and previous histories were not stated.

Four months previously she had noticed that the angle of the left scapula was enlarged, and did not feel natural. Five weeks previously she had noticed a lump in her left axilla. There was no spontaneous pain, and only over the scapula was there tenderness on pressure. Up to the time when she entered the hospital the growth had gradually increased. She had gained, rather than lost, weight.

The physical examination showed the patient to be rather thin. Her eyes and throat were normal. The base of the neck on the left side, just above the clavicle, bulged. In the left breast was the scar of an old complete breast operation for adenocarcinoma, which was undoubtedly the primary growth from which the metastases affecting neck, axilla, and scapula spread. There was increased resistance to percussion over the left pulmonary apex and the clavicle. The respiratory sounds were faint in the same area. Just above the left clavicle there was a firm mass of enlarged glands 2×3 cm. in size. Motion and sensation in the left arm were almost entirely absent.

The lower half of the scapula was enlarged by the presence of an ovoid, elongated mass, 6×10 cm. in size.

Hesitation was felt about undertaking an operation in this case, because it was impossible to predict the extent of the growth under the scapula. The patient's general condition was good, and as the pain was intense from pressure against the brachial plexus, it was finally decided to make a partial resection of the shoulder, carrying the operation into the axilla from behind as far as need be.

An incision was made over the anterior border of the scapula. On developing the operative field it was found that the lower part of the scapula was between two massive layers of the growth. A Gigli saw was passed underneath it, at a safe distance from the growth, and the bone divided. The huge mass of bone and tumor was then dissected away, but it was found that it extended high up into the posterior space of the axilla, growing firmly against the axillary artery from behind, and involving the scar of the first operation in front. For three quarters of an inch the artery was so hemmed in by the growth that the latter could not be entirely removed without removing a portion of the vessel. " Crile " clamps were applied to the artery both below and above the affected part, and when the vessel was divided near each, the entire mass was removed from the patient. Then, by shifting the position of the external jugular vein and throwing the arm slightly backward, it was possible to approximate the severed ends of the vessel. By employing the Carrel technic, using a No. 16 needle and divided silk thread, as described elsewhere in these pages, no difficulty was encountered in making a tight connection. In fact, except for the awkwardness of the position in which it was necessary to work, it was not nearly so difficult as anastomosing two smaller vessels would have been. On removing the clamps the stream flowed across without a drop of blood escaping. The pulse appeared at the wrist, although feebly. The patient endured the operation well.

It should be stated here that the urgent indication for the reëstablishment of the continuity of the axillary artery was that in the first operation on the breast the anterior collateral circulation was destroyed, and in the second operation the posterior collateral circulation was also destroyed. By the elimination of both it was absolutely necessary to maintain the main circulation in order to preserve the arm.

The work of Gaylord and Clowes, Ehrlich, and others has shown that if mice with carcinoma are bled there is a more rapid de-

velopment of the growth. It was felt that it might, therefore, be possible, as there was a certain loss of blood during the operation, that the growth of any remaining cancer cells might be stimulated, while if an abundant supply of new blood were added, their growth might be inhibited. On this ground transfusion was proposed.

A sister of the patient served as donor. She was forty-five years of age, and in good health. One of her radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for eight minutes under 150 mm. of pressure in the donor's vessels.

Immediately after the onset of the transfusion the patient complained of great pain in the back, precordial distress, and nausea. She expectorated considerable glairy sputum, and became somewhat cyanotic. This was due to slight temporary acute dilatation of the heart. On being taken to the ward she had a chill, and two hours later her temperature was 100.8° F., and she perspired freely. There was no blood pigment in the urine, nor was there any evidence of nephritis, the amount of fever was no greater than often occurs after transfusion, or saline infusion. Moreover, there was a steady increase in the number of red cells—from 2,400,000 to 2,600,000 immediately after the transfusion, and by the end of one hundred and twenty hours up to 4,000,000. The hemoglobin showed a corresponding rise.

At the present time, eleven months after the operation, the growth has recurred, although the patient is still living. The circulation is still maintained in the left axillary artery, as is shown by the persistence of the radial pulse and the persistence of the functions of the arm.

Comment.—The effect of the transfusion on the growth itself was negative—at least, as far as the final outcome was concerned. Whether it was retarded at all or not cannot be stated. The probability is that it was not, the careful dissection having removed all the visible growth. This case is an excellent illustration of the successful application of the methods of Carrel, Guthrie, and others in permanently reuniting a severed blood-vessel.

The statistics are as follows:

The Donor

Time	Red Count	Hemoglobin	White Count
Before transfusion.	5,550,000	100%	6,400
After transfusion.	5,440,000	100%	9,280

(See Chart, Fig. 10, p. 95.)

Case No. IV, 2 (6,851). Abstract. Consultation with Dr. W. F. Golling, Bedford, Ohio.

Epithelioma of the Hard Palate; Excision; First Transfusion; X-ray Treatment; Second Transfusion after Three Months; Effect of Transfusions on Growth of Tumor Entirely Negative.

The patient was an American, forty years of age, with a negative family history. His previous history was negative in its bearing on the tumor of the upper jaw of which he complained.

Three months previously he had noticed a pea-sized nodule on the inner side of the left upper gum opposite the first molar tooth. It was a fungoid growth, freely movable, bled easily, and was not attached to the underlying bone. It gradually encroached on the hard palate and along the jaw until it reached the size it had at the time when it was removed. Five weeks previously a physician had removed a portion of it. At about the time when it was first noticed bloody pus was discharged from the nose for several days. The patient had lost ten pounds in weight.

A fungoid tumor, $4 \times 2 \times \frac{1}{2}$ cm., was found to occupy the left half of the hard palate and extend slightly over on the alveolar border and the cheek. The cheek was swollen on the exterior, and the mass was firmly attached to the bone. One enlarged gland was found over the carotid artery at the angle of the jaw, and two of the posterior cervical glands were enlarged.

The tumor and glands were carefully excised as completely as possible. Then a transfusion was performed, with the hope that the patient might acquire immunity.

A sister-in-law of the patient served as donor. One of her radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for fourteen minutes.

The patient's face filled out, his color improved, the red count rose from 3,912,000 to 4,240,000, the hemoglobin from 70 to 80 per cent, and the white count fell from 14,000 to 11,040. The blood-pressure only rose 10 mm. He felt decidedly stimulated and re-

freshed. The blood condition was sustained, and later rose to normal, no hemolysis occurring, but the tumor continued to grow as rapidly as before, and the therapeutic value of the transfusion in affecting the growth was absolutely negative.

A second transfusion from another donor was performed about three months after the first one. Beyond the fact that it was entirely uneventful, no further statement can be made, as the records were lost. As before, the effect on the growth was negative. As it could not be completely removed at the operation, what was left grew steadily, in spite of long-continued X-ray treatments.

Comment.—The result obtained in this case was entirely negative.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Before transfusion.	3,912,000	70%	14,000
After transfusion.	4,240,000	80%	11,040
1st day.	4,160,000	80%	12,800
2d day.	4,240,000	....	12,000
4th day.	4,320,000	80%	13,200
5th day.	4,620,000	80%	12,040
6th day.	4,980,000	....	10,080
7th day.	4,900,000	90%	14,600
8th day.	4,940,000	....	......
10th day.	5,006,000	100%	15,200
11th day.	4,920,000	100%	14,000

(See Chart, Fig. 53.)

Case No. IV, 3 (6,899). Abstract. Consultation with Dr. D. C. Hughes, Findlay, Ohio.

Epithelioma of the Upper Jaw, with Metastases in the Neck, and Well-developed Cachexia; Excision of the Tumor at First Operation; Wound Left Open for X-ray Treatments for Two Months; Block Incision of Glands of Neck and Closure of Opening in Cheek into Mouth at Second Operation; Continued X-ray Treatments; Transfusion Forty-six Days after Second Operation; Temporary Improvement; Recurrence of the Disease Six Months Later at Site of Scar of Original Tumor; Death at End of Nine Months.

The patient was an American, thirty-six years of age, who had been struck on the left cheek with a rod six months previously. His family and personal history were both negative.

Following the injury a rapidly growing tumor of the upper jaw had developed, which involved the alveolar border of the teeth, ex-

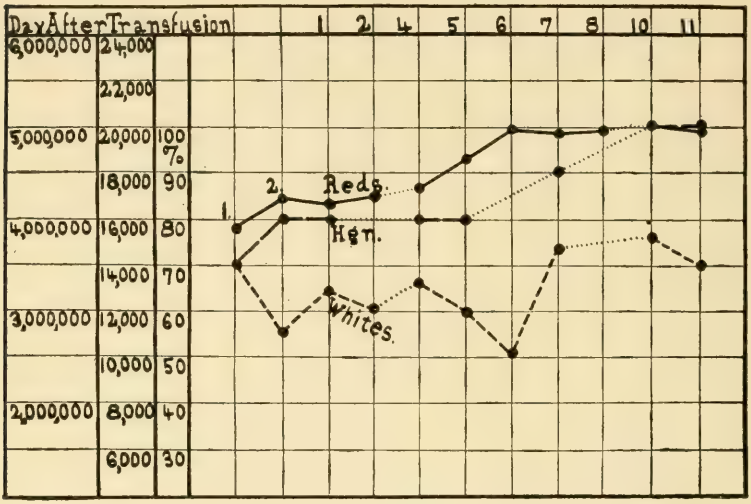


FIG. 53.—CASE NO. IV, 2 (6,851), FIRST TRANSFUSION. BLOOD CHART OF RECIPIENT. EPITHELIOMA OF HARD PALATE. 1, 2. Just before, and just after transfusion. Duration of transfusion, fourteen minutes.

tended across the palate to near the median line, and also involved the antrum and the greater part of the bony structure of the upper jaw and the soft parts of the cheek. It seemed to be an incurable case, but on account of the great suffering, the foul discharge, and the patient's desire to seize any remote chance of cure which might offer, it was decided to operate. The pathologist reported the tumor to be an epithelioma. The glands in the neck were found to be involved.

At the first operation the upper respiratory passages were thoroughly sprayed with albolene, the patient was anesthetized by means of pharyngeal tubage, and the left carotid artery was exposed and temporarily closed with a "Crile" clamp. Thus hemorrhage was minimized and the inhalation of blood prevented. The patient endured the operation well and made a prompt recovery. No attempt was made to remove the glands at this operation.

At the second operation, which was done two months later, a complete block excision of the neck was made. Great difficulty was encountered in doing this, as the X-ray treatments had caused great

hyperemia, and proliferation of connective tissue. The patient also endured the second operation well.

In spite of the extensive dissection of face and neck, and the vigorous use of the X-ray, it was felt that probably some cancerous tissue still remained. Consequently, forty-six days after the second operation, it was decided to transfuse, both because the patient was anemic, and because it was desired to test the effect of transfusion in such a case.

The donor was a brother of the patient. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for about thirty-five minutes.

The patient's face became well filled out, his lips and ears became quite pink, and he showed general evidence of having received a large amount of blood. His blood-pressure rose 10 mm., his pulse fell from 108 to 96, and his respirations fell from 28 to 20. He felt very much invigorated. As soon as the donor began to show the effects of losing the blood the flow was stopped. He left the hospital that day, and felt no ill effects.

While the patient stayed in the hospital he gained in weight. The blood and urine showed no evidence of hemolysis. At the end of two weeks he was sent home. At this time a suspicious-looking ulcer, about 1 cm. in diameter, was noticed at the antero-lateral aspect of the hard palate. For a time he felt stronger and his appetite improved, but the growth soon returned, and spread with great rapidity. Death occurred nine months after his first entrance to the hospital.

Comment.—In this case there was no evidence to show that the new blood exerted the least favorable influence on the growth. The physical condition was temporarily improved, but that was all. No hemolysis occurred.

The statistics of the donor are as follows:

The Donor

Time	Red Count	Hemoglobin	White Count
Before transfusion.	5,240,000	100%	8,000
After transfusion.	5,200,000	100%	11,040
1st day.	4,980,000	90%	9,000

(See Chart, Fig. 11, p. 97.)

Case No. IV, 4 (7,117). Abstract.

Inoperable Carcinoma of the Groin Metastatic from the Scrotum; Transfusion on Three Separate Occasions from Five Different Donors in a Period of One Hundred and One Days; No Hemolysis after First Two Transfusions; Hemolysis after Third Transfusion; Death Ten Days after Third Transfusion; Cause of Death not Definitely Known; Effect of Transfusion on Carcinoma Entirely Negative.

The patient was an American, fifty-one years of age, whose complaint was pain in his abdomen. His family had no history of neoplasm, tuberculosis, or hemophilia. His father died of pneumonia and his mother of diabetes mellitus. Three brothers were alive and well. He had had malaria for twenty-seven years, rheumatism on two occasions, and the usual diseases of childhood. He denied having had venereal disease.

Seven years previously he had first noticed a wart on the right side of his scrotum, which grew to be the size of a walnut in two years. This was cauterized, and the scrotum and right testicle were removed one year later. Six months previously the inguinal glands on both sides had been removed. Two months previously he had begun to have pain in the left groin, which was worse at night. His legs ached down to his knees. He lost thirty pounds in weight in one month.

On making the physical examination nothing abnormal was found in the thorax. The abdomen was full and tympanitic in the flanks, but was not tender, and no masses could be found. No glands could be palpated in either groin. The right leg and groin were swollen and tender. The diagnosis of carcinoma of the groin and thigh was made, and confirmed later by microscopical examination. As the case was clearly an inoperable one, transfusion was proposed as a tentative measure, and the proposal accepted by the patient.

First Transfusion.—A young man in good condition, who was not related to the patient, served as donor. One of his radial arteries was anastomosed to a superficial vein of the patient near the elbow by the cannula method. From another vein 600 c.c. of blood were removed before the transfusion was begun. The donor's radial artery was very small, so that the flow was correspondingly small, also. The blood was allowed to flow across for seventeen minutes.

In spite of the amount of transfused blood being small, the immediate effect was very stimulating. The red count rose from

4,736,000 to 4,880,000, the hemoglobin from 80 to 90 per cent, and the white count from 6,000 to 9,040. As no observations were made before the preliminary bleeding, it is not known what effect it had or how much blood was replaced by the transfusion. There were no gross symptoms of hemolysis—no fever beyond what would have been expected from the transfusion alone, no jaundice, and no discoloration of the urine.

On the thirteenth day after the transfusion considerable serum was aspirated from the region of the groin. It was an orange-red, turbid fluid, and apparently bloody. Cultures taken from it were sterile. On heating portions of it, and also after adding acetic acid, it coagulated almost completely. By the forty-eighth day after the transfusion there had been no visible improvement in the condition of the groin and thigh, and, in fact, the condition was worse, as there was more swelling and it had gone on to ulceration of the surface, with a profuse, foul-smelling discharge. In spite of the fact that there had been no change for the better in the growth, the patient insisted that he obtained enough relief from the first transfusion to make it worth while to undertake a second.

Second Transfusion.—At the second transfusion two donors were used. The first donor was a young man who was not related to the patient. He weighed 154 pounds before the transfusion, and lost $4\frac{3}{4}$ pounds during his part of it. The second donor was also a young man who was not related to the patient. He weighed 165 pounds before the transfusion, and lost 3 pounds.

A radial artery of the first donor was anastomosed to a superficial vein of the patient near the elbow by the cannula method as before. His blood was allowed to flow across for about sixty minutes. Then the second donor was connected in the same way to the same vein, and the blood allowed to flow across for about twenty minutes.

Before the first donor's blood was allowed to flow across, the patient was bled 1,600 c.c. from his right radial artery. This resulted in marked depression, wrinkling of the face, pallor, free perspiration, running pulse, restlessness, and air-hunger. There was a little delay in connecting the first donor, and in the short interval of waiting 650 c.c. of normal saline solution were given intravenously. The patient was also put into an exaggerated Trendelenburg position. The effect of the infusion in improving the general condition was slight. Making the anastomosis was rendered exceptionally difficult owing to the first donor having a double radial artery. As the transfusion progressed the symptoms of hemorrhage gradually

lessened, and the Trendelenburg position was changed accordingly. The first donor brought back the patient to about the condition before the bleeding. Then the second donor was attached. The patient's condition improved still more, and he felt well in every way; the stimulation which he received was really remarkable. His face was filled out and red, while his pulse and respiration were normal. The time spent in performing the whole operation was about five hours.

Eighteen hours after the second transfusion the patient had a severe chill. There was no headache, pain, jaundice, or blood in the urine. The appetite was poor, and he felt more or less chilly all day. Forty-eight hours later he felt very well. From that time on until the third transfusion there were alternating periods of his feeling well and feeling badly. The discharge from the groin became very foul, and recurred after a thorough curetting under nitrous-oxid anesthesia. The progress was steadily downward. It was only too evident that the transfusions had no effect in checking the growth, but in spite of this the patient again insisted that he had been enough benefited on the two previous occasions to make it worth while to try a third time.

Third Transfusion.—At the third transfusion two more donors were used. They were both young men in good condition, and were not related to the patient. The details of the transfusion were the same as before. Blood was allowed to flow across for forty minutes from the first donor and thirty-four minutes from the second.

Before the first donor was connected to the patient, the latter was bled just as freely as possible, 1,650 c.c. being removed. About 1,000 c.c. of saline infusion were given before the transfusion was begun. For the full details of the bleeding and subsequent transfusion, page 90 *et seq.*, should be consulted. The immediate recovery was excellent.

On the second day after the transfusion the patient was slightly jaundiced. He was nauseated, and vomited occasionally. His urine showed the presence of a slight amount of hemoglobin, and the dressings of the wounds in the arm were stained with a profuse, bright red discharge. The red count began to fall. On the third day there was more jaundice and more hemoglobin in the urine. The jaundice was a bronzing rather than the yellowish discoloration such as is due to obstruction of the bile ducts. From this time on the symptoms increased. The urine became scanty, the stomach continued to be upset so that nutrient enemata had to be given, the

edema in the groin and thigh increased, and the pain became more and more severe. Death occurred on the tenth day. An autopsy could not be obtained. The cause of death is discussed under Chapter XV, page 309.

Comment. — This case affords a most striking example of the inefficiency of transfusion in treating cancer. The blood from 5 different donors transfused on 3 different occasions had absolutely no effect in checking the course of the disease. While such a negative result is most disappointing, it is of decided value in showing one of the limitations of transfusion. The hemolysis gave the clew to the study of this phenomenon as a possible aid to the diagnosis of cancer from study of the blood.

The statistics are as follows:

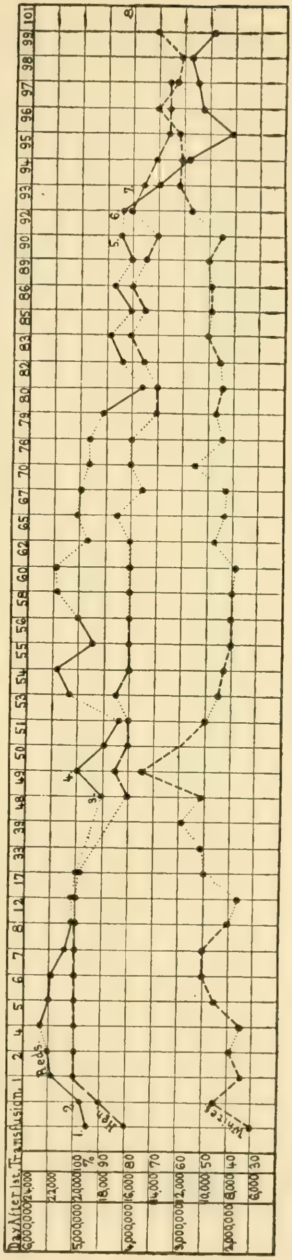


FIG. 54.—CASE NO. IV, 4 (7,117). BLOOD CHART OF RECIPIENT. CARCINOMA OF THE GROIN. TRANSFUSIONS FROM FIVE DONORS. 1, 2. Day before, and immediately after first transfusion (bled 600 c.c., and transfused for seventeen minutes from one donor). 3, 4. Day before, and shortly after second transfusion (bled 1,600 c.c., gave 650 c.c. saline infusion, and transfused for about eighty minutes from two donors). 5, 6. Day before, and day after third transfusion (bled 1,650 c.c., gave 1,000 c.c. saline infusion, and transfused for seventy-four minutes from two donors). 7. Jaundice (hemolysis). 8. Death.

THE RECIPIENT

First Transfusion

Time	Red Count	Hemoglobin	White Count	Remarks
Day before.	4,736,000	80%	6,000	
Just after.	4,880,000	90%	9,040	
1st day.	5,440,000	100%	7,000	
2d day.	5,520,000	100%	7,800	
4th day.	5,660,000	100%	7,000	
5th day.	5,504,000	100%	9,000	
6th day.	5,480,000	100%	10,000	
7th day.	5,200,000	100%	10,000	
8th day.	5,080,000	100%	8,400	
12th day.	5,076,000	100%	7,400	
17th day.	4,986,000	100%	10,000	
33d day.	....	.....	10,200	
39th day.	....	.....	11,800	
48th day.	4,500,000	80%	10,200	Day before second transfusion.
		Second Transfusion		
49th day.	5,020,000	85%	15,000	The counts were made shortly after second transfusion.
50th day.	4,480,000	80%	12,000	
51st day.	4,160,000	80%	10,000	
53d day.	5,120,000	85%	9,000	
54th day.	5,400,000	80%	8,600	
55th day.	4,700,000	80%	8,000	
56th day.	5,000,000	80%	8,000	
58th day.	5,400,000	80%	8,000	
60th day.	5,440,000	80%	7,800	
62d day.	4,800,000	80%	9,400	
65th day.	5,000,000	85%	8,600	
67th day.	4,992,000	75%	8,500	
70th day.	4,800,000	80%	11,000	
76th day.	4,800,000	80%	8,800	
79th day.	4,564,000	70%	9,400	
80th day.	3,800,000	70%	8,800	
82d day.	4,168,000	75%	9,000	
83d day.	4,400,000	80%	10,000	
85th day.	4,000,000	75%	9,800	
86th day.	4,320,000	80%	9,600	
89th day.	4,000,000	75%	10,000	
90th day.	4,200,000	70%	9,000	
		Third Transfusion		
91st day.	....	.....	......	Day of third transfusion.
92d day.	4,160,000	80%	11,200	
93d day.	3,456,000	75%	12,200	
94th day.	2,900,000	70%	12,000	
95th day.	2,000,000	65%	12,200	
96th day.	2,600,000	65%	14,000	
97th day.	2,700,000	65%	12,500	
98th day.	2,856,000	.....	12,000	
99th day.	2,416,000	.....	14,000	

(See Chart, Fig. 54.)

Case No. IV, 5 (7,118). Abstract. Consultation with Dr. H. C. Crumrine, of Cleveland, and Dr. E. A. Weeks, Akron, Ohio.

Carcinoma of the Kidney in an Eighteen-months-old Child; Nephrectomy; Transfusion; No Recurrence until after Lapse of Eight Months.

The patient was an eighteen-months-old child with an abdominal tumor. One of his great-grandfathers died of cancer. His family had no other history of neoplasm, and no history of hemophilia or tuberculosis. Except that he had had a week of gastrointestinal disturbance a year previously, and pneumonia five months previously, his personal history was negative.

For four months he had had many gastrointestinal attacks with diarrhea, vomiting, and indigestion. His abdomen began to swell gradually, and a tumor was noticed in his right side. The right upper quadrant of the abdomen had finally become greatly distended. He had had frequency of micturition, but no blood had been noticed in his urine.

The physical examination showed the baby to be thin and pale. The cardiac dullness extended 1 cm. to the left of the nipple line, and a sharp diastolic murmur could be heard over the entire precordia. In the right half of the abdomen a tumor could be palpated which extended into the flank. The veins in the abdominal wall above it were markedly distended. The kidney could not be palpated. The diagnosis of renal tumor was made. It was decided to transfuse after operating, in order not only to influence any possibly unremoved growth, but to overcome shock if induced by the operation.

An incision over the most prominent part of the tumor was carefully made after the patient's father had been made ready to act as donor. The tumor was removed without incident. With the kidney it measured 13 × 10 × 8 cm., and had several knobs. No evidence of metastasis was found. The pathologist later reported it to be a carcinoma.

Just as soon as the operation was completed, the father's exposed radial artery was quickly anastomosed to a median basilic vein of the patient by the cannula method, without difficulty, the vein being cuffed back on the cannula and the artery drawn over. The blood was allowed to flow across for about twenty minutes, the pressure being regulated with great care to avoid acute cardiac dilatation.

The baby's features were colored and well filled out by the new blood. No exact blood determinations were made. The pulse rate was decreased and the blood-pressure increased. In short, he was raised from a poor circulatory condition to a good enough one to permit his being returned to bed and placed in the head-up position.

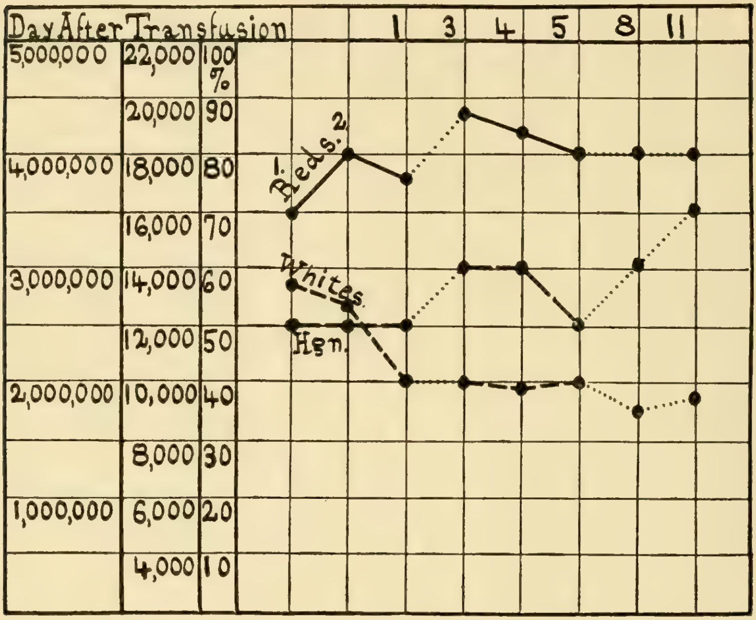


FIG. 55.—CASE NO. IV, 5 (7,118). BLOOD CHART OF RECIPIENT. RENAL CARCINOMA. 1, 2. Day before, and just after transfusion. Duration of transfusion about twenty minutes.

The immediate convalescence was very prompt and satisfactory. For eight months there was no sign of recurrence, but after that it became evident.

Comment.—Transfusion made the removal of the carcinoma technically safe, but did not prevent recurrence. This case illustrates the fact that vascular anastomosis may be safely accomplished even in an 18-months-old child.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Day before.	3,500,000	50%	13,500
Just after.	4,000,000	50%	12,800
1st day.	3,800,000	50%	10,000
3d day.	4,380,000	60%	10,000
4th day.	4,200,000	60%	9,800
5th day.	4,000,000	50%	10,000
8th day.	4,000,000	60%	9,000
11th day.	4,000,000	70%	9,400

(See Chart, Fig. 55.)

SUMMARY

CASE NO. IV, 1 (6,850).

Transfused.—For adenocarcinoma of the axilla and scapula.

Immediate Result.—Improvement in general condition.

Other Treatment.—Thorough operative removal of growth.

Late Result.—Recurrence at the end of eleven months.

CASE NO. IV, 2 (6,851).

Transfused.—For epithelioma of the hard palate, on two occasions with interval of three months.

Immediate Result.—Decided general improvement.

Other Treatment.—Excision of tumor and lymphatic glands before first transfusion; X-rays.

Late Result.—The growth continued.

CASE NO. IV, 3 (6,899).

Transfused.—For epithelioma of upper jaw with metastases in the neck.

Immediate Result.—General improvement.

Other Treatment.—Local excision, block dissection of neck two months later; X-rays.

Late Result.—Recurrence at end of six months, death at end of nine months.

Case No. IV, 4 (7,117).

Transfused.—For inoperable carcinoma of groin metastatic from the scrotum. There were 3 separate transfusions from 5 different donors in a period of one hundred and one days.

Immediate Results.—General improvement after first and second transfusions, hemolysis after third transfusion.

Other Treatment.—Extensive bleeding before each transfusion.

Late Result.—Death ten days after third transfusion from a combination of causes, among which "hemolysis" doubtless played a part.

Case No. IV, 5 (7,118).

Transfused.—For carcinoma of kidney in an infant.

Immediate Result.—General improvement.

Other Treatment.—Nephrectomy.

Late Result.—Patient living. Growth recurred after eight months.

Other cases in which carcinoma was present are V, 3 (7,108), VIII, 4 (6,849), VIII, 6 (6,898), IX, 2 (6,852), IX, 13 (6,605), and IX, 18 (7,439).

CONCLUSIONS

Transfusion has no effect in checking the growth of carcinoma.

CHAPTER XXI

EXOPHTHALMIC GOITER

(Group V)

Case No. V, 1 (6,162). Abstract.

Exophthalmic Goiter with Very Marked Symptoms of Toxemia, Delirium, etc.; Failure of Medical Treatment; Transfusion Attempted from an Unsuitable Donor; Flow Begun, but Stopped on Account of Donor; Death of Patient in a Few Hours.

The patient was an American woman, thirty-five years of age. Her mother and one niece had goiter. A sister died of tuberculosis. Otherwise the family history was negative. The patient had had the ordinary diseases of childhood, and had always been well except for the trouble under discussion. She had had three normal confinements.

She had had a goiter since she was a child, but exophthalmic symptoms had not developed until two years previously, following childbirth. At times the symptoms would be very slight. Again, without apparent cause, they would be very much aggravated. She was very nervous, felt depressed mentally, worried and cried easily, had asthma, palpitation of the heart, a good deal of headache, and considerable numbness in her arms and legs. Up to six months previously she had lost 40 pounds in weight, but in the next four months this had all been regained.

The physical examination showed her to be a slight, poorly nourished woman. There was no glandular enlargement. The reflexes were normal. Her hands had a fine tremor, her eyes protruded, von Graefe's and Stellwag's signs were present, and she had a symmetrically enlarged thyroid gland. The vessels in the neck pulsated forcibly, and a thrill was both palpable and audible. The pulse was 140 per minute, easily compressible, and a little irregular. The blood-pressure ranged from 80 to 95 mm.

The patient was put to bed and given atropin for eight days. The pulse and blood-pressure remained about the same, but the mental condition became much worse. She was almost uncontrollable,

cried a great deal, had delusions of persecution, and slept very little. Two nights before the transfusion she was in such bad condition that she nearly died. As it was evident that all resources had been exhausted that were then at command, it was finally decided to try transfusion, on the ground that new blood might sufficiently diminish or overcome the toxemia so that she would become a surgical risk. This was proposed as a purely tentative measure, and in view of the extreme gravity of the situation was so accepted by the husband of the patient.

On the morning of the transfusion the patient was so wildly delirious that even under large doses of morphin it was impossible to make the anastomosis between her and her husband's vessels. She was therefore given ether, and a radial artery of the husband anastomosed to one of her superficial veins near the elbow by the suture method. This was no sooner accomplished and the flow begun than it was decided that it was best not to continue, on account of the poor condition and nervousness of the husband, who had atheromatous vessels and an organic lesion of the heart. He was the only donor who could be obtained at the time. Therefore the transfusion was terminated before sufficient blood passed over to give a fair test of what might be accomplished with its aid. The condition of the patient was unaffected, and death occurred a few hours later.

Comment.—This was the first case in which, as far as can be ascertained, transfusion by direct anastomosis of the vascular system of one human individual to another was ever attempted. In the light of later experience, it is strongly felt that if the flow had been allowed to continue no harm would have resulted. At the time it was thought wisest to err on the safe side on account of the condition of the donor.

Case No. V, 2 (7,105). Abstract. Consultation with Dr. W. E. Lower.

Exophthalmic Goiter with Marked Toxic Symptoms; Operation under Cocain Anesthesia; Critical Condition of Patient; Transfusion and Simultaneous Bleeding; Acute Cardiac Dilatation; Death in a Little More Than Two Hours After Transfusion.

The patient was an American woman, twenty-three years of age, who complained of having an enlarged neck. Her family and per-

sonal history were negative. Her menstruation had always been normal until the trouble under discussion began.

A year previously she had first noticed that her pulse was rapid. At this time the thyroid enlargement had probably been present for some time. Two months later she noticed that her legs trembled after she had stood up for a short time, and soon after that her fingers were tremulous. Since six months previously she had not menstruated for more than three days at each period, where she formerly had flowed for a week. She did not know of any fright having preceded the onset of the first symptoms, although she had had a miscarriage when four months pregnant three months before the onset. In the last three weeks before entering the hospital she had taken thyroid extract.

The physical examination showed the patient to be fairly well nourished. There were no signs of anemia, cyanosis, or edema. Both her tonsils were enlarged. In the anterior part of the neck there were two masses, one on each side of the median line. The right was 9 cm., and the left 8 cm., in diameter. They were of firm consistency and with fairly definite outlines. The eyes reacted to light and distance. There was slight, if any, exophthalmos. Von Graefe's sign was absent. The outstretched fingers showed a fine tremor. The knee jerks were slightly exaggerated. The heart and lungs showed no abnormalities except that the action of the former was rapid.

On the fourth day before the operation the patient was put on Beebe's serum. She had had several attacks of palpitation and precordial distress for which no immediate exciting cause could be found. They all came on after she ate her breakfast. When washed by the nurse before breakfast all unnecessary manipulation was avoided, and the neck was handled as little as possible. On the morning of this particular day the pulse rose to 208 beats per minute at the maximum, and varied between 208 and 168. It was irregular in force and rhythm. The blood pressure at the time when taken was 115 mm. The patient was extremely nervous, making restless movements of her hands and feet, and complaining bitterly of feeling nervous. The skin was covered with irregular erythematous blotches which came and went. The hands and feet were cold. After about fifteen minutes the symptoms grew milder, the pulse rate coming down to 140, and the nervous feeling disappearing, but she was more or less upset for the entire morning. At times her cerebration was abnormal and there was a mild degree of toxic delirium.

In getting the patient ready for operation there was a delay of about twenty minutes. When placed on the table she was talking volubly, and almost immediately became delirious. After ten minutes she became quiet, and the operation was begun under cocain. The right lobe was first removed, and then part of the left, in the usual way. The tissues were everywhere very vascular, and the bleeding was profuse. Ineffectual attempts were made to control it with cautery and suture, but oozing continued from the skin and muscles and she showed marked toxic symptoms. It was decided to bleed and then transfuse.

The patient's husband served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. On cutting down to the vein it was found to be collapsed, and from all the tissues there was rapid exudation. When the anastomosis was completed the patient's blood-pressure was 118, the respiration 45 per minute, and the pulse 178 per minute.

Before the flow was allowed to begin the pulse had fallen to 160. As the blood passed over the patient was bled from one of her radial arteries at a rate which was as near the rate of flow of the incoming blood as could be determined. In all 800 c.c. of blood were removed. The pulse soon went up to 198 per minute, cyanosis developed, and the right heart dilated out 6 cm. to the right of the sternum. The blood was allowed to escape more freely from the radial artery in order to reduce the pressure still more. Rhythmic massage was maintained over the sternum. The transfusion was stopped. The pulse was then 204 per minute. The wound in the neck had been packed to stop the hemorrhage, but without much effect. It was then repacked, after first taking numerous running sutures in the tissues without avail, and finally controlled. The patient was returned to the ward in a critical condition at 12 M. At 12.45 her temperature was 105.6° F.

She was soon very cyanotic, the pulse running at about 200 per minute, and very weak. Massage over the heart was given at intervals. Death occurred at 2.10 P.M., a little over two hours after the transfusion. At 2.20 the body temperature was 107° and at 2.45 P.M. 107.4° per rectum.

Comment.—The hope that the introduction of new blood after bleeding the patient would so dilute the toxins that their effect would be lessened or avoided was not realized, as was shown by her failing to respond at all to the treatment. In

fact, the question may very properly be raised as to whether actual harm was not done by causing dilatation of the heart by the introduction of the new blood in greater quantity than it could endure in its weakened condition. It is considered that the psychic element had a very strong and very unfavorable effect in causing the fatal outcome.

Case No. V, 3 (7,108). Abstract. Consultation with Dr. G. F. Zinninger, Canton, Ohio.

Exophthalmic Goiter; Adenocarcinoma of Breast and Axilla; Patient in Poor Condition; Removal of Goiter under Cocain Anesthesia; Patient Transfused for Stimulating Effect to Prepare for Amputation of Breast; Excellent Recovery; One Month Later Carcinoma Removed; Excellent Recovery; Gain of 30 Pounds in Weight and No Recurrence of Carcinoma at End of Four Months.

The patient was an American woman, fifty-three years of age, who complained of having a goiter, and a tumor in her left breast. Her father died of old age, her mother of "paralysis," one brother of pulmonary tuberculosis, another of typhoid fever, a third of "convulsions," several cousins of pulmonary tuberculosis, a grandmother of epithelioma of the nose, and three sisters of "flux," a disease characterized by violent abdominal cramps and very bloody stools. A sister was being treated for cancer (the part of the body affected was not stated), and a brother for pulmonary tuberculosis. Her eleven remaining living brothers were not in good health.

The patient herself had had measles, scarlet fever, varicella, influenza, and "flux." She had been troubled for years with nasal catarrh which had affected her hearing, palpitation of the heart with rapid pulse, dizziness, and dyspnea, and chronic gastric indigestion and constipation. Her stools had frequently been of a greenish color, and she had had attacks of jaundice.

Two and a half years previously she had first noticed a swelling in the front of her neck, although the area in which it came had always been tender on pressure. Her heart became irregular in its action, beat rapidly, and throbbed after any excitement. The slightest pressure on her neck caused great pain. About two years previously she first noticed a swelling in the left breast, which caused darting pains which were made worse whenever she had gas in her

stomach. Up to the time of entrance she had lost over 100 pounds in weight.

The physical examination showed the patient to be of a nervous temperament, emaciated, and very restless. Her skin was moist. Her pulse was 128 per minute, of low tension, but regular. In the inner and upper quadrant of the left breast was a nodular mass which seemed to be rather definite in outline and not adherent to the nipple. It was about 7 cm. in circumference, hard, and tender on pressure. In the axilla and over the clavicle enlarged glands could be palpated. The thyroid gland was much enlarged, of rather soft consistency, and tender on pressure. The extended fingers showed a fine tremor. The epigastric region was extremely tender on pressure. There seemed to be a mass along the lower border of the stomach. It was not well defined, and was quite painful on pressure. The right heart was dilated ½ cm. to the right of the sternal border. At the apex there was a loud blowing systolic murmur. The second pulmonic sound was accentuated.

Under cocain anesthesia a circular incision was made around the goiter and the larger part of it was removed without difficulty in the usual way. The patient endured the operation well, but as the operation on the breast remained to be done, it was decided to transfuse in order to help her over the immediate effects of the removal of the goiter and shorten the interval necessary before removing the breast tumor. Her previous physical condition made her a very poor risk for the second more severe operation. The pathologist reported the goiter to be between the exophthalmic and the colloidal type, but nearer the former. It was not malignant.

The husband of the patient served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The blood was allowed to flow across for about twenty-four minutes.

The transfusion was uneventful. The patient was markedly stimulated, as it was hoped that she would be. Her face became fuller, her lips and other mucous membranes pinker, her pulse fell in rate and increased in volume, and she made a splendid recovery from the operation. A month later the breast was amputated with dissection of the glands. The tumor was found to be an adenocarcinoma. The patient endured this operation well also. Since then she has gained 30 pounds in weight, has improved very much in her general condition, and has had no sign of recurrence. Up to the present time, four months after the breast amputation, the supposed mass affecting the stomach has caused no further trouble.

Comment.—This case was an excellent illustration of the stimulating effects of new blood. The transfusion was really done neither for exophthalmic goiter nor carcinoma, and there was little or no shock after the first operation. The increased vitality was what was desired. For lack of a better place, the case has been classified in this group. Judging from other experiences in transfusing in cases of carcinoma, any ultimate freedom from recurrence of the carcinoma will depend entirely on the thoroughness of the operation, and not on the transfusion itself.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Just after.	4,528,000	70%	6,600
1st day.	5,016,000	....	11,000
3d day.	5,464,000	....	9,000
5th day.	5,143,000	....	8,600

SUMMARY

CASE NO. V, 1 (6,162).

Transfused.—For exophthalmic goiter with patient in a very toxic condition.

Immediate Result.—The transfusion had to be discontinued on account of the condition of the donor, no result for the time which it lasted.

Other Treatment.—None subsequent to transfusion.

Late Result.— Death of patient a few hours after transfusion.

Note.—This, as stated elsewhere, was hardly a fair test of the effect of transfused blood on exophthalmic goiter.

Case No. V, 2 (7,105).

Transfused.—For exophthalmic goiter with patient in a very toxic condition.

Immediate Result.—Acute cardiac dilatation; no improvement.

Other Treatment.—Excision of all but a portion of the left lobe of the thyroid; bleeding before the transfusion.

Late Result.—Death of patient at end of two hours.

Case No. V, 3 (7,108).

Transfused.—To improve general condition of a patient with both exophthalmic goiter and adenocarcinoma of breast and axilla.

Immediate Result.—Marked stimulation, and beginning general improvement.

Other Treatment.—Goiter removed before the transfusion, breast removed one month later.

Late Result.—No sign of recurrence of carcinoma at end of four months after the breast amputation. At that time the patient had gained 30 pounds in weight and was in excellent condition.

CONCLUSIONS

In exophthalmic goiter the negative results following transfusion, with or without preliminary bleeding, seem to indicate that the toxic substances present in this condition are in rather stable combination with the fixed tissues. Therefore transfusion with or without bleeding does not afford relief.

CHAPTER XXII

TUBERCULOSIS

(*Group VI*)

Case No. VI, 1 (2,047L). Abstract. Consultation with Dr. W. E. Lower.

Tuberculosis of Kidney; Nephrotomy; Drainage of Large Abscess; Transfusion; Temporary General Improvement; No Effect on Discharge of Pus; Return of Patient to Former Condition after About Two Weeks.

The patient was an American woman, twenty-two years of age. Her mother, two maternal uncles, and one of her grandfathers died of pulmonary tuberculosis. Her father was living and well. There was no history of cancer. As a child the patient was not very strong. Her menstruation began at about fifteen years, lasted for ten weeks, and then stopped for one year. It then continued for eight weeks, and stopped for about nine months. Since then it had been fairly regular.

When seventeen years old the patient began to have frequent urination following colds, which was accompanied by burning, scalding pain. About one month later she had had pain in her left side which lasted for twenty-four hours. She never passed any blood. She then had occasional pain in her side, but did not vomit. She was treated for bladder trouble and had her bladder washed out. She had been married about three and a half months previously. Six weeks previously she caught cold, and had subsequently been more or less bedridden.

After a cystoscopic examination and catheterization of the ureters by Dr. Lower, the diagnosis of tuberculosis of the left kidney was made. Tubercle bacilli were found in the urine. By an oblique incision along the border of the twelfth rib the kidney was exposed and incised and a large abscess evacuated. The pus had a fecal odor. Owing to the poor general condition of the patient, and the hope that new blood would help her to overcome the infection, a transfusion was performed by Dr. Lower and the author.

The patient's husband served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the suture method. The flow was allowed to continue for forty-four minutes.

The condition of the patient immediately began to improve as the transfusion progressed. Her face filled out gradually and became pinker, her pulse became slower, and the blood-pressure rose. Immediately after the transfusion she had a slight chill.

She gained very much in strength and spirits, and for about two weeks her initial improvement was more than maintained. Soon after, however, she gradually lost ground and returned to her former condition. Apparently the suppuration did not diminish.

Comment.—As far as favorably influencing the tuberculous process was concerned, the effect of the transfusion was apparently negative.

The statistics of the donor are as follows:

The Donor

Time	Red Count	Hemoglobin	White Count
Before transfusion.	5,840,000	90%	8,500
End of 15 minutes.	5,232,000	80%	5,700
End of 30 minutes.	4,328,000	75%	......
End of 45 minutes.	4,800,000	73%	8,900
End of 1° 50′.	5,640,000	75%	8,800
End of 3° 20′.	4,500,000	73%	9,200
End of 4° 20′.	4,800,000	75%	8,500
End of 5° 20′.	4,608,000	75%	8,400
First day.	4,752,000	80%	10,400

(See Chart, Fig. 12, p. 99.)

CASE NO. VI, 2 (6,718). ABSTRACT. CONSULTATION WITH DR. W. W. HOLLIDAY.

Probable Pulmonary Tuberculosis; Pleurisy with Effusion; Tuberculous Peritonitis with Effusion; Drainage of Chest and Abdomen; Reaccumulation of Fluid in Each Place; Second Drainage; Transfusion; Reaccumulation of Fluid in Abdomen and Drainage on Two More Occasions; Gain in Patient's Weight for Six Weeks; Eventually Apparent Recovery.

The patient was an American, seventeen years of age, with a negative family history. As a child he had chicken-pox, measles, and

pertussis with good recoveries. Three months previously he had had a febrile attack with night sweats, chills, a rapid pulse, and cough. He also had burning after micturition. The diagnosis of typhoid fever was made, but there were no rose spots. No Widal reaction was sought for. Two months previously he had noticed that his abdomen was swollen, but his feet were not swollen at this time. When he coughed he had had pain in his left side just below the ribs.

The physical examination showed the presence of fluid in both the right chest and in the abdomen, with probably a tuberculous process in the right apex. The abdomen was opened and a large amount of fluid removed. The diagnosis of tuberculous peritonitis was confirmed. At about the same time the chest was tapped and fluid removed from that also. The patient was not at all benefited by these procedures, as there was a rapid reaccumulation even after the chest and abdomen were tapped a second time. Transfusion was then suggested on the hypothesis that new blood might result in the invading bacteria being overcome, especially as there was both marked emaciation and anemia present.

The donor was a normal, healthy male who was not related to the patient. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method. The blood was allowed to flow across for thirty minutes.

During the transfusion the patient had some precordial distress and was markedly cyanotic. He coughed and vomited, the pulse rose to 132 per minute, and the respirations were rapid. The right heart was considerably dilated, but not far enough to make it necessary to bleed in order to lower the pressure to give relief. In the light of later experience there is no doubt that the patient should first have been bled before adding so large a volume of blood to the circulation. He stated that his hands, toes, and ears, which had been cold for months, became warm after the transfusion; they remained so for several months.

The patient gained in weight for six weeks after the transfusion, but since that time the abdomen has filled up twice more, and has been operated on and drained each time. Later the patient apparently made a good recovery.

Comment.—It may be properly inquired whether or not a preliminary bleeding and a slower transfusion might not have obviated the cardiac dilatation. Improvement was marked,

but other treatment alone may have accomplished it. The effect of transfusion in this case may be inferred after a wider experience.

Case No. VI, 3 (7,372). Abstract. Consultation with Dr. W. W. Holliday.

Pleurisy with Effusion; Extensive Tuberculous Peritonitis and Salpingitis; Aspiration of Chest with Removal of 500 c.c. of Fluid; Transfusion; Improvement of Patient's Bodily but not Mental Condition; Laparotomy; Removal of One Fallopian Tube; Abdomen Drained; Gush of Fecal Matter from Wound Nineteen Days after Operation; Death Two Days Later; No Autopsy.

The patient was an American woman, twenty-one years of age, who complained of having fever. Her family history was negative as regards tuberculosis, neoplasm, or hemophilia. As a child she had had diphtheria and measles. Two years previously she had had pleurisy of the right side which lasted a week. Her menstruation had always been regular. She had never had any vaginal discharge.

Three months previously she began to feel tired, have pain in her legs and abdomen, headache, chills and fever, and be constipated. After a month she went to bed and had been confined to her bed up to the time she entered the hospital. She continued to have a fluctuating fever with pain in the left side at the level of the lower ribs, which was made worse when she took a full breath. There was no localized abdominal pain.

The physical examination showed the patient to be pale and emaciated. The spaces between her left lower ribs bulged, and there were the other typical signs of a pleuritic effusion, including dullness of the paravertebral angle. The abdomen was domed, and everywhere tympanitic. The muscles were tense throughout. In the left iliac fossa there was a certain amount of fullness. The liver and spleen were not palpable. The vaginal examination showed a tender mass connected with the uterus on the right side. The left part of the vaginal vault was indefinitely swollen, indurated, and tender.

Immediately after the physical examination was completed the left chest was aspirated. Five hundred cubic centimeters of turbid, dark straw-colored fluid were obtained. The patient coughed a little during the aspiration. By night she was able to breathe much more easily and felt relieved. By reason of the presence of what was doubtless a tuberculous process in the chest, and because tuberculous

peritonitis was suspected, it was decided to transfuse, hoping not only to affect the tuberculous process but to place the patient in better condition before performing a laparotomy.

The husband of the patient served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The blood was allowed to flow across for thirty-one minutes. As the flow was strong, the artery was compressed somewhat to reduce it. The husband showed no effects from the loss of blood. The patient was not bled before transfusing.

When the transfusion was begun the patient was trembling and apparently somewhat delirious, as she kept muttering to herself. Her face was cold, her pulse weak, 148 per minute, and of poor volume. After the transfusion the pulse had risen to 160 per minute, but was of much better quality. The face was distinctly flushed. There was no acute cardiac dilatation. The psychic condition did not change. The patient talked continually, repeating everything that was said in the room. Her hearing seemed to be very acute for distant sounds, while near ones seemed to be heard as if far away. The pupils were widely dilated, the eyelids twitched continuously, the eyes showed no intelligence of what was being done, but stared with an anxious expression. She did not vomit, and had no chill or pulmonary edema. Her bodily condition was very much improved.

Under light anesthesia the abdomen was opened by a median incision. About a liter of clear fluid escaped. The peritoneum was everywhere studded with small tubercles. Both Fallopian tubes showed marked tuberculous involvement with caseous masses protruding from the end of each. The right tube was rapidly excised, but the left was left in place. Drainage was inserted and the wound partly closed around it. The patient's pulse was very rapid, but of good volume and tension. She soon began to talk just as she did before the operation.

On the nineteenth day after the operation there was suddenly a gush of fecal matter from the lower part of the abdominal wound, which had been kept open up to that time. Two days later death occurred. An autopsy was not permitted.

Comment.—The tuberculous involvement was very great. While marked bodily improvement followed the transfusion, it had no effect on the mental changes or in delaying the fatal outcome.

Case No. VI, 4 (7,417). Abstract.

Tuberculous Peritonitis and Salpingitis; Transfusion; Development of Dyspnea, Cyanosis, and Rapid Pulse without Dilatation of Right Heart; No Previous or Subsequent Evidence of Hemolysis; Double Salpingectomy; Apparent Complete Recovery at End of Fourteen Months.

The patient was an American woman, twenty-nine years of age, who complained of pain in her back and stomach. Her family history was negative for tuberculosis, neoplasm, and hemophilia. When young she had had scarlatina, parotitis, and chicken-pox. A year previously she had had a slight attack of pleurisy.

On entrance the physical signs indicated the presence of free fluid in her right chest and in her abdomen. The latter was tender all over, but no masses could be felt. It was decided to transfuse, and then perform a laparotomy.

Previous to the transfusion the hemolysis tests showed no hemolysis, reverse hemolysis, or autolysis. The husband served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The blood was allowed to flow across for eight minutes.

When the transfusion had progressed for four minutes the recipient complained of inability to breathe. Marked dyspnea appeared, with cyanosis and a small rapid pulse. The right heart did not become dilated. Raising the patient to the head-up posture did not give relief, so the flow was stopped. The patient had a slight chill at once. It was thought that the husband's blood was somewhat toxic to the patient, although nothing was shown *in vitro* which would indicate this to be the fact.

Immediately after the transfusion the abdomen was opened by a median incision below the umbilicus. The intestines were found to be everywhere matted together and studded with tubercles. No free fluid was found, as it was thought would be from the physical signs. Both Fallopian tubes were swollen and filled with necrotic material. They were removed, a large iodoform gauze drain inserted in an opening made into the vagina through Douglas's pouch, and the abdomen was closed in layers. The patient endured the operation well. Thirty-three days later she was discharged from the hospital in good condition. The pathologist reported the process to be tuberculous. Fourteen months later the patient was still well.

Comment.—The complete recovery was so unexpectedly rapid that the transfusion may fairly be credited to have been an important factor.

SUMMARY

CASE No. VI, 1 (2,047L).

Transfused.—For general effect on a discharging tuberculous abscess of the kidney.

Immediate Result.—General improvement for about two weeks.

Other Treatment.—Nephrotomy, drainage of abscess.

Late Result.—No effect on the process.

CASE No. VI, 2 (6,718).

Transfused.—For tuberculous peritonitis, pleurisy with effusion and probable pulmonary tuberculosis.

Immediate Result.—Gain in weight for six weeks.

Other Treatment.—Chest and abdomen tapped, dietetic.

Late Result.—Reaccumulation of fluid, but eventually apparently good recovery.

CASE No. VI, 3 (7,372).

Transfused.—For extensive tuberculous peritonitis, pleurisy with effusion.

Immediate Result.—Improvement of bodily but not of mental condition.

Other Treatment.—Chest tapped before transfusion, after transfusion laparotomy and drainage, removal of one Fallopian tube.

Late Result.—Gush of fecal matter from abdomen at end of nineteen days; death on twenty-second day.

CASE No. VI, 4 (7,417).

Transfused.—For tuberculous peritonitis and salpingitis.

Immediate Result.—Inconsequential.

Other Treatment.—Laparotomy; double salpingectomy.

Late Result.—Patient discharged at end of thirty-three days in good condition.

Other cases in which tuberculous conditions were present are VIII, 8 (7,109) and IX, 9 (6,663).

CONCLUSIONS

In cases of tuberculous peritonitis the operative risk is greatly improved by transfusion. Moreover, it seems quite certain that transfusion has more than a temporary effect on the tuberculous process itself. As it has been demonstrated that the opsonic index is lowered in tuberculosis, it would seem that improvement following transfusion might be attributable, at least in part, to the increase in the opsonic content of the blood of the recipient. Is it possible that immune bodies exist in nontuberculous subjects? If they do exist, are they in the blood, and to what extent?

CHAPTER XXIII

CHRONIC SUPPURATION

(*Group VII*)

CASE NO. VII, 1 (7,125). ABSTRACT. CONSULTATION WITH DRS. H. A. FIESTER AND L. G. LELAND, NEWTON FALLS, OHIO.

Infected Multilocular Cyst of Broad Ligament; Patient in Comatose Condition; Laparotomy; Evacuation of Cyst; Vaginal Puncture and Drainage; Patient in Shock; Transfusion; Slight Improvement; Death on Ninth Day after Transfusion.

The patient was an American woman, twenty-nine years of age, who was brought to the hospital in a comatose condition.

Her physician stated that her abdomen had been enlarged for three years. It had been tapped several times, a clear fluid resembling urine being withdrawn. The patient had had slight fever (never more than 1° F.) and at times had been delirious. Recently she had had difficulty in taking food, and had eaten almost nothing for a week. She had had a small movement of the bowels the day before, and had passed no urine since the night before. The menstruation had been regular but scanty. During the periods she was very nervous.

When the patient was examined the comatose condition persisted. Subsultus tendinum was present. The temperature was 101° F., the pulse 140 per minute and of poor volume and tension. The pupils were dilated. They reacted very sluggishly to light, but not to distance. The lungs were clear except for a few crackling râles at the bases. The point of maximum impulse of the heart was diffused over an area several centimeters square. Dullness extended 8 cm. to the left of the mid-sternal line. The heart sounds were clear, but feeble. The abdomen was markedly distended in an asymmetrical way, the point of maximum distention being in the left hypochondrium. There was tympany in the left flank, and dullness, with a fluid wave, in the left hypochondrium. The ankles were slightly edematous.

A median incision was made below the umbilicus, and through it a huge multilocular cyst of the broad ligament was found to be present. Many of the upper loculi were emptied of a viscid fluid. When the lower ones were opened, pus with the typical colon bacillus odor came out. A vaginal puncture was made and a large rubber drainage tube inserted. At the end of the operation the patient was in a state of shock. Transfusion was performed to relieve it and assist if possible in overcoming the infection.

The husband of the patient served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The vein was cuffed back over the cannula and the artery slipped over it. The blood was allowed to flow across for twenty-five minutes.

During the transfusion the patient's pulse became slower and the tension and volume improved. She was returned to her room in fairly good condition, the shock being lessened. She did not respond as well to the transfusion as it was hoped she would, however. The drainage from the vagina was profuse and very foul.

For nine days the patient lingered along with rapid weak pulse, nocturnal delirium, and subnormal temperature. On the ninth day the temperature rose to 103° F., and death occurred. The discharge from the vagina continued undiminished.

Comment.—The transfusion had no effect on the severe septic process. The patient was too profoundly affected to obtain anything more than slight immediate relief in combating the shock accentuated by the septicemia.

Case No. VII, 2 (6,698). Abstract. Consultation with Dr. L. E. Siegelstein.

Chronic Retroperitoneal and Broad Ligament Infection; Failure of Ordinary Methods of Treatment; Transfusion; Condition Unimproved.

The patient was a woman of unstated age who some time previously had been seized with an attack of chills and fever after an apparently normal confinement. At the time no evidence of pelvic inflammation could be discovered. The chills and fever continued for several months until she entered the hospital. There a large amount of pus was evacuated from the region of the left iliac fossa by an extraperitoneal incision. The peritoneal cavity was not opened at

any time, and the patient never had peritonitis. After employing various forms of treatment for several months—postural and ordinary drainage, baths, packs, medication, fresh air, etc.—it was found impossible to influence the persistent retroperitoneal and broad ligament infection which was present. Transfusion was, therefore, proposed with the hope that it might give the patient enough of a start toward recovery to lead to it eventually.

The husband served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method. The blood was allowed to flow across for twenty-five minutes. Before the flow began the patient was bled 500 c.c.

After the transfusion the patient felt better immediately, and her vital forces were distinctly improved. She slowly gained in weight after this, but a study of her condition for several months led to the conclusion that the transfusion did not alter the natural course of the suppuration, and was therefore distinctly negative in value.

Comment.—Transfusion did not control the chronic infection.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
21 days before.	4,464,000	80%	15,200
Before bleeding.	4,416,000	75%	18,000
After bleeding.	4,320,000	60%	22,000
After transfusion.	4,480,000	80%	17,400
1st day.	4,472,000	85%	20,000
2d day.	4,400,000	85%	18,000
3d day.	4,460,000	85%	16,040
4th day.	4,926,000	85%	17,140
5th day.	4,200,000	80%	16,200
7th day.	4,420,000	80%	15,000
8th day.	4,546,000	80%	14,040
9th day.	4,636,000	80%	13,880
10th day.	4,500,000	....	16,400
12th day.	4,620,000	80%	16,000
13th day.	4,700,000	85%	15,400
15th day.	4,640,000	85%	15,840
17th day.	4,580,000	85%	16,040

(See Chart, Fig. 56.)

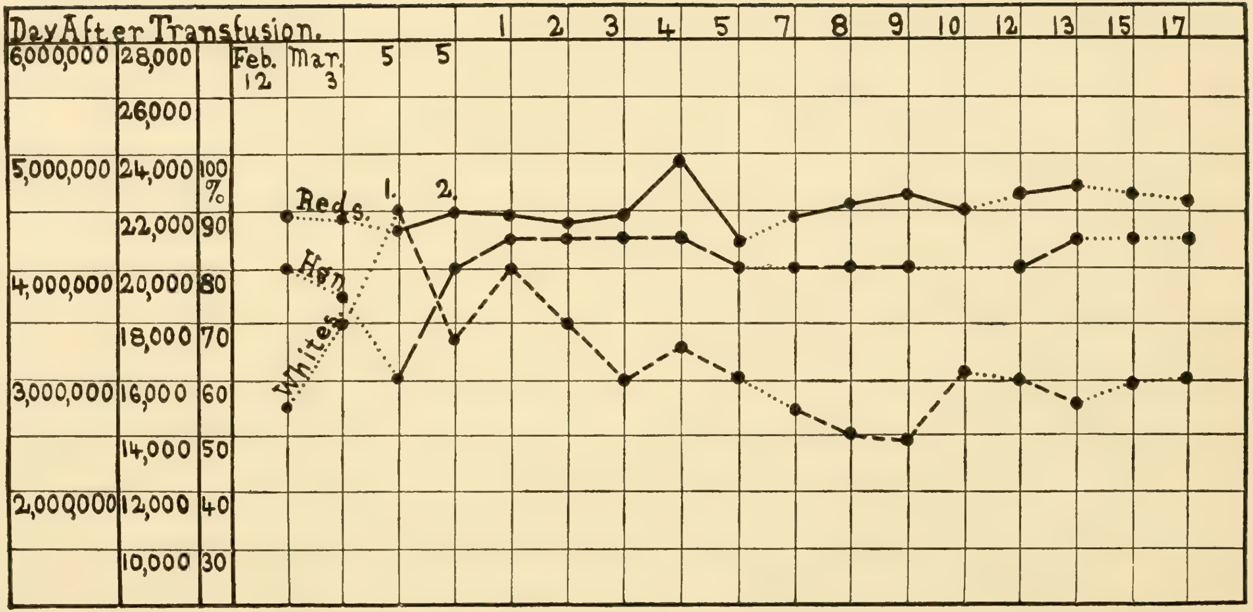


Fig. 56.—Case No. VII, 2 (6,698). Blood Chart of Recipient. Retroperitoneal Abscess. 1. Just after bleeding 500 c.c. (note characteristic fall in red cells and hemoglobin, and rise in white cells) and just before transfusion. 2. After transfusion. Duration of transfusion, twenty-five minutes.

The Donor

Time	Red Count	Hemoglobin	White Count
26 days before.	4,832,000	100%	11,120
2 days before.	4,980,000	85%	7,440
Just after transfusion.	4,860,000	90%	14,680
1st day.	4,448,000	90%	10,400
3d day.	4,480,000	90%	8,740
5th day.	4,620,000	90%	6,940
7th day.	4,600,000	90%	6,000
12th day.	4,840,000	100%	7,420

(See Chart, Fig. 13, p. 101.)

Case No. VII, 3 (6,696). Abstract. Consultation with Dr. J. A. Stephens.

Chronic Suppuration in a Child for One Year from Renal Abscess of Traumatic Origin; Emaciation and Weakness; Transfusion; Marked General Improvement; Nitrous-Oxid Anesthesia and Enlargement of Sinus; Gain of 20 Per Cent Body Weight in Three Weeks; Nephrectomy after Six Weeks; Complete Recovery.

The patient was a Hebrew boy, nine years of age. About a year previously he had received a severe injury to his abdomen, which caused a rupture of the right kidney and reduced him to a condition of profound shock. The kidney was exposed, the hemorrhage arrested, and the wound packed. Through the wound pus and urine were discharged, and finally a permanent sinus was formed. He had continuous fever, and was very much emaciated and anemic.

When he presented himself at the hospital the above conditions were present, and the signs pointed to the presence of a large suppurative mass in the region of the affected kidney. His pulse varied from 120 to 150, and was thready and weak, but regular. He was in the last stages of chronic suppuration, too weak to endure operation, and yet without it unable to make further progress toward recovery.

After observing him for several days, it was decided that the condition could best be dealt with by transfusion, followed by the establishment of freer drainage under nitrous-oxid gas if enough improvement followed the former to warrant it being undertaken. A brother served as donor. One of his radial arteries was anastomosed

to a venous branch of the patient near the elbow by the suture method. The blood was allowed to flow for twenty-two minutes.

During the transfusion the patient was very nervous and could only be controlled with great difficulty. He complained of great pain in his chest and back, his respirations quickened to 40 per minute, and he coughed considerably. These symptoms were thought to be due to acute dilatation of the heart. Accordingly he was placed in the head-up position, and the flow stopped temporarily in order to give the heart time to become adjusted to the increased blood mass. Before this was done he was nauseated, and vomited 3 ounces of clear gray fluid. He recovered in a very short time, and the flow was allowed to continue. A very marked improvement followed, so that it was possible to follow the original plan and increase the drainage opening under nitrous-oxid anesthesia. A large pocket of pus was found in the kidney.

Following the transfusion the patient gained 14 pounds in weight in three weeks—about one fifth of his total weight. A small sinus over the kidney remained, however. He was watched for a number of weeks, and when it was found that he had apparently reached the maximum in weight and strength without the sinus becoming obliterated, he was brought back to the hospital in six weeks to have the kidney removed.

At the operation it was found that the liver was displaced toward the median line. The kidney was very much enlarged, attached to the diaphragm, and extended well down below the costal border. The dissection was an extremely difficult one. The production of considerable shock could not be avoided. The entire organ was finally removed and the wound drained. The patient made an uninterrupted recovery, and is now in good health.

Comment.—The remarkable gain in the patient's weight was very striking. Apparently the new blood gave just the needed stimulus after the long period of decline under toxic conditions. While not enough to lead to obliteration of the sinus, the improvement rendered the immediate and the later operations feasible. Doubtless part of the initial improvement was due to the evacuation of pus from the kidney, but it cannot all be ascribed to that when the improvement obtained in other cases in which no pus was removed is considered.

The statistics are as follows:

The Recipient

TIME	Red Count	Hemoglobin	White Count
Day before.	4,216,000	70%	20,000
Just after.	4,290,000	70%	13,200
1st day.	4,248,000	70%	16,000
2d day.	4,360,000	70%	12,000
3d day.	4,280,000	70%	13,400
5th day.	3,728,000	70%	12,480
7th day.	3,860,000	70%	14,260
9th day.	4,240,000	70%	15,020
12th day.	4,200,000	70%	14,200
15th day.	4,290,000	70%	12,440
18th day.	4,320,000	70%	12,000
20th day.	4,608,000	75%	14,000

(See Chart, Fig. 57.)

The Donor

TIME	Red Count	Hemoglobin	White Count
Day before.	4,880,000	90%	10,000
Just after.	4,800,000	90%	14,000
10.00 P.M.	4,670,000	85%	10,800
1st day.	5,120,000	90%	9,000
7th day.	5,184,000	90%	6,440

(See Chart, Fig. 14, p. 103.)

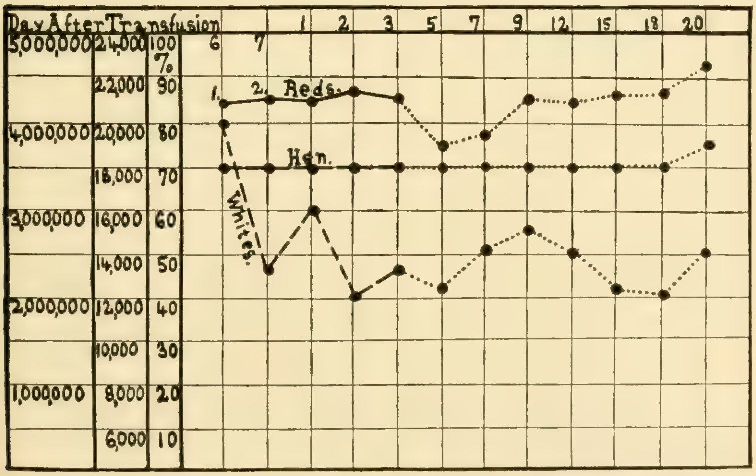


FIG. 57.—CASE NO. VII, 3 (6,696). BLOOD CHART OF RECIPIENT. CHRONIC SUPPURATION FROM RENAL ABSCESS. 1, 2. Day before, and just after transfusion. Duration of transfusion, twenty-two minutes.

SUMMARY

Case No. VII, 1 (7,125).

Transfused.—For chronic suppuration associated with infected multilocular cyst of broad ligament.

Immediate Result.—Considerable improvement.

Other Treatment.—Evacuation of cyst, drainage through vaginal puncture.

Late Result.—Death on ninth day after transfusion.

Case No. VII, 2 (6,698).

Transfused.—For chronic retroperitoneal and broad ligament infection.

Immediate Result.—Temporary improvement.

Other Treatment.—Preliminary bleeding; no operation.

Late Result.—Entirely negative after elapse of several months.

Case No. VII, 3 (6,696).

Transfused.—For chronic suppuration in a child, due to a renal abscess of traumatic origin.

Immediate Result.—Marked general improvement with gain of 20 per cent of body weight in three weeks.

Other Treatment.—Nephrectomy six weeks after transfusion.

Late Result.—Complete recovery.

Other cases in which chronic infection was present are VIII, 1 (6,695), VIII, 2 (7,122), and VIII, 4 (6,849).

CASES FROM OTHER SOURCES

Case A. Barwell.

The patient was a male, forty-four years of age, with a fracture of the tibia and fibula at the junction of the middle and lower thirds, and a jagged external wound. There was history of alcohol-

ism. The case was treated antiseptically. Suppuration set in, and union did not occur. About two months after the accident the necrosed ends of the tibia were sawed off and the leg reset, but repair was very slow. The granulations were pale and flabby, and the general condition was steadily growing worse—anemia, loss of appetite, local pain, etc. One month after the operation $8\frac{1}{3}$ ounces of human blood were injected intravenously into the forearm of the patient by Dr. Roussel. "During the operation the patient's eyes became markedly bright and fuller, and his face flushed; his skin became warm and moist, after a while perspiring freely; the pulse became fuller and stronger, and fell to 95. He complained of fullness and oppression at the chest. . . . He had some sense of fullness down the spine and aching at the loins. . . . The granulations at the seat of fracture, which previously were pale and flabby, were now well colored and of good consistence. . . . About half an hour after he was put to bed he had a slight rigor, soon followed by another, and shortly after by copious perspiration. He felt very thirsty. Had no pain or discomfort. . . . The urine was abundant, odorous, loaded with lithates of a very light pink, but was perfectly free from either blood or albumin. In the evening his temperature was 102° F." Two weeks after the transfusion the wound in the leg was healing well, and there seemed to be some union between the bones. A little over a month after the transfusion the patient was doing "perfectly well." To quote the author's summary: "Previous to transfusion the man's vital forces under the influences of shock of the accident, sloughing of soft parts, necrosis of bone, operation, and very free discharge, were rapidly giving way—threatened, indeed, if the same rate of diminution continued, to become before long extinct. From the moment when he received fresh blood, all these conditions were changed. His strength, the action of his circulatory system and of his assimilative powers, have been restored. Any embarrassment, traceable in the headache, nausea, and coated tongue, points rather to excess of blood than to debility. . . ."

CASE B. MUMFORD.[1]

Low Grade Sepsis Following Fracture of Pelvis and Rupture of Bladder; Exploratory Laparotomy, Suprapubic Cystotomy, and Perineal Section; Sixteen Days Later Pus Pocket in Perineal Wound Drained; Second Pocket Opened Next Day; Persistence

[1] The account of this case was received in a personal communication from Dr. R. B. Greenough, Boston, Mass.

of High Temperature; Transfusion; Condition About the Same; Four Days Later Another Pus Pocket Evacuated; Improvement; Patient Discharged Twenty-four Days Later.

The patient was a male, twenty-two years of age (Mass. Gen'l Hospital, No. 156,575).

"January 11, 1908. The patient was struck by a train and sustained rupture of the bladder and fracture of the pelvis.

"January 13th. Exploratory laparotomy, suprapubic cystotomy, and perineal section.

"January 29th. Small pocket of pus in perineal wound drained.

"January 30th. Another pus pocket drained. The temperature remains high and the patient is in poor condition.

"February 3d. Transfusion done by Dr. J. G. Mumford under cocain. Radial artery of donor connected with the median basilic vein of patient. The connection remained for twenty-five minutes. The donor's pulse went from 88 to 96. The patient's pulse went from 108 to 126. The condition remained about the same.

"February 7th. Another pus pocket opened. After this the patient gained, and is discharged much improved to the convalescent home, April 2d."

CONCLUSION

In cases of chronic suppuration transfusion may cause a marked increase in the vitality of the patient.

CHAPTER XXIV

SHOCK AND COLLAPSE

(*Group VIII*)

CASE No. VIII, 1 (6,695). ABSTRACT. CONSULTATION WITH DR. H. POMEROY, CHARDON, OHIO.

Actinomycotic Abscess in True Pelvis; Drainage through Vagina; Collapse of Patient; Transfusion; Resuscitation; Death Four Weeks after Transfusion; Extensive Morbid Processes Discovered at Autopsy.

The patient was an American woman, forty years of age, with negative family history. She had had the usual diseases of childhood, typhoid fever when three years old, dysentery at ten and eighteen years, and ear trouble which followed measles at ten and had persisted ever since. At twenty she had puerperal eclampsia, at twenty-five a miscarriage, and at thirty-two a yellowish-white, non-offensive, non-irritating discharge suddenly began from the vagina and had persisted ever since. At the same time the menstruation began to be painful on the first day of every period. She had one twelve-year-old child.

For the four previous years she had had fainting attacks which usually occurred at the rate of 3 a month. After an attack she was sometimes unconscious for an hour, but she did not bite her tongue nor froth at the mouth, and felt perfectly well as soon as she was conscious. Three years previously she was curetted in the hope of obtaining relief. After this the discharge became foul and profuse. Since that time she had had fever, great pain, and no return of the menstruation, and was confined to her bed. She had lost considerable weight.

The patient was found to be very weak and emaciated—in fact, she was reduced almost to a skeleton. The abdomen was a little full over the right iliac fossa, and tender all over. The tenderness was greatest over the iliac fossæ and the region of the symphysis pubis.

The feet were somewhat edematous. The diagnosis of pelvic abscess was made.

Under nitrous-oxid anesthesia a vaginal puncture was made, and then a transverse incision behind the cervix into the *cul-de-sac* of Douglas. About 200 c.c. of foul-smelling bloody pus were evacuated. The odor was distinctly fecal, but no sinus or fistula could be found. At the beginning of the operation the patient's pulse was 130 and at the end 160. As she was in extremely poor condition and rapidly failing, it was decided to perform a transfusion.

The husband of the patient served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method. When the transfusion began the vein was dilated to twice the size of the artery and pulsated strongly. The flow was allowed to continue for thirty-six minutes.

As a result of the transfusion the patient's color improved, the waxy hue disappeared, she moved her eyes and smiled at those around her, and her face was less drawn. The impending dissolution was checked, and her general condition was better than it had been for several weeks prior to her coming to the hospital.

The improvement was maintained for several days, and then she began to lose ground. The amount of discharge from the pelvis was very great. Eleven days later thrombosis of the left femoral vein developed. Death occurred four weeks after the transfusion.

At the autopsy a huge abscess cavity was found occupying the true pelvis. The tip of the appendix extended over the brim of the pelvis and into the abscess cavity. The right Fallopian tube was chronically inflamed, while the left tube and the uterus were normal. It was impossible to say whether the infection originally came via the right tube or appendix. Sections of the tissue showed actinomycosis hominis to be present. One of the ovaries was filled with actinomycotic abscesses. Other conditions present were subacute and chronic peritonitis, thrombosis of the left external iliac vein, marked fatty degeneration of the liver, and chronic interstitial and parenchymatous nephritis.

Comment.—Transfusion helped to tide over the crisis which occurred when the necessity of performing the vaginal puncture arose, but it did not suffice to do more than this in the presence of such extensive and varied morbid conditions.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count	Remarks
Day before.	....	....	7,040	
3.00 P.M.	2,040,000	30%	7,180	Before transfusion.
5.40 P.M.	2,069,000	42%	7,200	After transfusion.
1st day.				
5.00 P.M.	2,464,000	55%	5,200	
11.00 P.M.	....	42%	.....	
2d day.	2,624,000	50%	14,400	
3d day.	2,972,000	50%	19,720	
4th day.	2,522,000	55%	20,000	
6th day.	2,016,000	50%	5,280	
8th day.	2,224,000	50%	6,840	
10th day.	2,680,000	50%	5,400	
12th day.	2,720,000	50%	7,240	
14th day.	2,408,000	60%	8,840	

(See Chart, Fig. 58.)

Differential Blood Counts Before and After the Transfusion

	Before	After
Polymorphonuclear neutrophiles...........	91.6%	89.0%
Small lymphocytes........................	3.6%	4.5%
Large lymphocytes........................	4.2%	5.6%
Transitional forms.......................	0.2%	0.5%
Eosinophiles.............................	0.0%	0.3%
Mast cells...............................	0.4%	0.0%
Total number leucocytes counted..........	477	377

The Donor

Time	Red Count	Hemoglobin	White Count	Remarks
3.30 P.M.	5,184,000	95%	10,760	Before the transfusion.
5.45 P.M.	4,920,000	65%	8,680	After the transfusion.
11.00 P.M.	4,600,000	....	13,920	
1st day.	4,208,000	80%	12,040	
2d day.	4,064,000	80%	12,840	
3d day.	4,768,000	90%	8,800	
4th day.	4,990,000	90%	9,600	
6th day.	5,312,000	100%	10,400	
10th day.	5,224,000	100%	9,040	

(See Chart, Fig. 15, p. 105.)

Differential Blood Counts Before and After the Transfusion

	Before	After
Polymorphonuclear neutrophiles	75.2%	76.1%
Small lymphocytes	9.1%	9.6%
Large lymphocytes	10.2%	7.6%
Transitional forms	1.5%	2.8%
Eosinophiles	2.0%	3.6%
Mast cells	0.6%	0.3%
Total number leucocytes counted	342	394

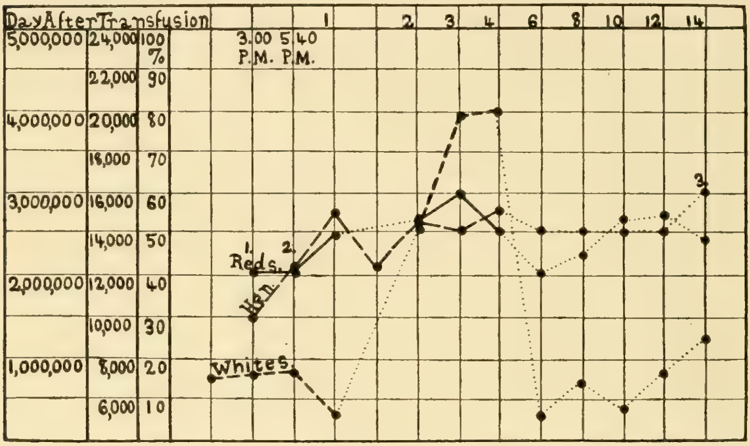


FIG. 58.—CASE NO. VIII, 1 (6,695). BLOOD CHART OF RECIPIENT. ACTINOMYCOSIS IN THE TRUE PELVIS. 1, 2. Before and after transfusion. 3. Death. Duration of transfusion, thirty-six minutes.

CASE NO. VIII, 2 (7,122). ABSTRACT. CONSULTATION WITH DR. J. A. KOEHLER, SHELBY, OHIO.

Sarcoma of Uterus and Ovaries Complicated with Severe Pyogenic Infection; Laparotomy; Panhysterectomy Begun; Sudden Collapse from Cardiac Failure; Artificial Respiration; Panhysterectomy Hastily Finished; Transfusion; Death of Patient Shortly after Transfusion; Autopsy not Permitted.

The patient was an American woman, fifty-nine years of age. Her mother and a brother had died of heart disease, her father of tuberculosis, and a sister of pneumonia. There was no history of

neoplasm or hemophilia. She herself had had "brain fever," several attacks of grippe, and the usual diseases of childhood.

About three months previously the patient weighed about 160 pounds. Suddenly, without apparent cause, she began to feel weak, suffer from dizziness and loss of appetite, and to lose weight. By the time she entered the hospital she had lost 45 pounds. She had constant headache. At first she slept well, but soon very little. Up to two weeks previously, there were no symptoms which suggested uterine disease. Attention was first called to it by dull abdominal pain. Examination then showed a growth to be either on or in the uterus. She vomited considerably, and had difficulty in passing her urine.

The physical examination showed the patient to be emaciated and anemic. Her forehead was slightly edematous. The heart and lungs were negative. There was no cyanosis or general glandular enlargement. In the abdomen a firm mass could be palpated which extended 10 cm. above the symphysis pubis in the median line.

At the operation a median incision was made over the tumor. The uterus was found to be much enlarged and rather soft, with marked pyogenic infection of the surrounding parts. The broad ligaments were clamped and divided. An incision was begun in the cervix, when suddenly the patient collapsed almost completely. The operation was hastily finished, artificial respiration was begun, and preparations were made for transfusion.

The husband of the patient served as donor. One of his radial arteries was rapidly anastomosed to a median basilic vein of the patient by the cannula method. The blood was allowed to flow across for about ten minutes.

The patient did not respond to the transfusion, and died about an hour later. An autopsy could not be obtained.

The pathologist reported that little, if any, of the uterine muscle had not been destroyed by the tumor, and that the ovaries were also completely involved. The histological examination showed the growth to be a spindle-celled sarcoma.

Comment.—This case is an example of a group in which transfusion can be of no service, viz., in cases of collapse from cardiac breakdown. It was only attempted here in sheer desperation and without much hope of benefit. It was decided merely to give it a trial, and, if the patient improved, to continue and give a full transfusion. It required only a few min-

utes to demonstrate clearly that the patient was not showing the usual response that is seen in suitable cases.

Case No. VIII, 3 (7,123). Abstract. Consultation with Dr. N. C. Yarian.

Complete Avulsion of Arm Above Elbow; Patient in Severe Shock; Removal of Remainder of Humerus by Disarticulation; Patient Returned to Ward in State of Shock; Slight Temporary Relief Obtained by Infusion of 1,000 c.c. Normal Saline Solution; Rapid Development of Still More Profound Shock; Transfusion; Immediate and Permanent Disappearance of Unfavorable Symptoms; Complete Recovery.

The patient was an American, twenty-nine years of age, who had had his arm torn off by a cogwheel. He was brought into the author's service at Lakeside Hospital from the ore docks in an ambulance. The left arm had been torn completely off, about 4 inches of the humerus being left intact and 3 more inches badly crushed. The remaining muscles were badly torn. There was very little hemorrhage, and the patient's companion said that there had been but little. The skin covering the arm was so completely torn off that there was not enough left to make a flap with which to cover the stump. He suffered great pain, and was very weak, the shock being severe.

The operation was performed by Dr. Yarian. Under gas and ether anesthesia the axillary artery and vein were first ligated, and the brachial plexus severed, after being blocked with cocain. The humerus was exposed and disarticulated, the muscles trimmed off, and the skin from in front of and to the rear of the wound brought into as good coaptation as possible. The wound was drained with a cigarette drain and dressed with a moist bichlorid dressing.

After the operation the patient was in still deeper shock. One thousand cubic centimeters of normal saline infusion improved the circulation temporarily, but he soon became worse. His pulse was 150 per minute, barely perceptible at the wrist, he was in a cold sweat, his complexion was of a pasty, pale hue, and his blood-pressure was down to 90 mm. mercury, and falling. He was at once taken back to the operating room and made ready for transfusion. The transfusion was performed by the author's house staff, Drs. Sloan and Gamble.

The donor was thirty years old, and weighed 190 pounds. One of his radial arteries was anastomosed to a median basilic vein of

the patient—the vein being cuffed back and the artery slipped over it. The vein was thick-walled, so that only a small amount of blood passed over. Consequently the anastomosis was separated and another thinner-walled vein used. The flow via the second vein was excellent, and was allowed to continue for thirty-five minutes, when the donor showed signs of distress by his increased respiratory rate and by restlessness.

The change in the patient was little short of remarkable. Instead of the picture of profound shock, he presented practically a normal appearance. His pulse had fallen from 156 to 110 per minute, the volume had increased, the tension had risen from 90 to 128 mm., the sweating had disappeared, the skin was dry, his mind was clear, and the stupor had passed away. He was returned to the ward in excellent condition.

The symptoms of shock never returned. On the twenty-fourth day after the transfusion he was discharged from the hospital. He had previouly been skin-grafted.

Comment.—This case illustrates the conclusions reached in the laboratory that transfusion may easily succeed when saline infusions completely fail.

The statistics are as follows:

THE RECIPIENT

During the Transfusion

Time		Pulse	Blood-Pressure
4.08 P.M.	Transfusion started........................	156	....
4.21 P.M.	Transfusion stopped........................	144	....
4.39 P.M.	Transfusion started again..................	140	....
4.47 P.M.		...	90 mm.
4.50 P.M.		132	....
4.55 P.M.		130	100 mm.
5.15 P.M.	Transfusion ended..........................	110	128 mm.

CASE NO. VIII, 4 (6,849). ABSTRACT. CONSULTATION WITH DR. C. H. CUSHING, ELYRIA, OHIO.

Infected Bilateral Multilocular Broad Ligament Cysts with Carcinomatous Degeneration, Carcinoma of Uterus and Sigmoid Flexure; Drainage and Excision of Cysts; Panhysterectomy; Ex-

cision of Portion of Sigmoid Flexure; Collapse of Patient; Transfusion; Revival; Death from Toxemia on Second Day after Transfusion.

The patient was an American woman, fifty-four years of age, with negative family and personal history as far as the trouble under discussion is concerned.

Four years previously her abdomen had become enlarged and the diagnosis of ovarian cyst had been made. After that time it steadily increased in size. She had no pain or discomfort, and only loss of strength and appetite until two months previously. Then she had chills, recurring fever, and increasing abdominal tenderness.

The patient was found to be pale and emaciated. The heart sounds were clear, but the action was very weak. The abdomen was dome-shaped below the umbilicus. A fluctuating oval mass, about 20 by 20 cm. and projecting 10 cm. above the normal level of the abdominal wall, could be palpated. Projecting loculi could be felt on its surface. Free fluid was present in the flanks. The vaginal examination showed the presence of a firmly fixed mass, occupying all of the true pelvis. The shins were not edematous.

The patient was an extremely poor risk, but owing to the rapid growth of the tumor in the past six weeks, the emaciation and symptoms of infection, and the fact that she was losing ground so rapidly, it was decided to take the chances of operation. At this time the presence of carcinoma was not suspected.

A 10-cm. incision was made to the left of the umbilicus. Later its length had to be doubled. The abdominal wall was very thin, and its layers could not be easily determined. The peritoneum was very much thickened. On incising it a thick-walled cyst was found to be adherent to it. The cyst was punctured, and three or four liters of purulent, thin, brown fluid, containing large white pieces of necrotic tissue, were withdrawn. It had an odor as if infected with Bacilli coli communis. After the cyst was emptied its inner surface was found to be lined with great flakes of necrotic membrane. It extended downward from the costal margin to the pelvis, and the greater part of it was readily peeled from the peritoneum with the fingers. On approaching the pelvis the upper abdomen was walled off with gauze. Smaller densely adherent cysts were found in the true pelvis. In freeing them, several exuded purulent contents. It was decided to perform a complete supravaginal hysterectomy. The patient was lowered from the Trendelenburg position to prevent drainage toward the diaphragm.

The left broad ligament was clamped and incised, and the inci-

sion carried across the cervix and up the other side, the uterus and appendages being thus removed. The bladder was found to be drawn well up on the cyst wall and held there by adhesions. These were quickly separated. The uterus was involved in carcinoma, and also part of the sigmoid flexure. In dissecting out the latter, a part of the sigmoid had to be excised, the cut ends being reunited by an end-to-end anastomosis. The raw surfaces left by the various incisions were obliterated by means of running and interrupted cat-gut sutures. A large caliber rubber drainage tube was inserted into the vagina through a puncture posterior to the cervix. The pelvis was flushed out with normal saline solution, and the abdomen rapidly closed. At the end of the operation the patient was in such severe shock as to be almost pulseless. The blood-pressure was 50 mm. Transfusion was advised.

A son-in-law of the patient acted as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for thirty-one minutes.

Within several minutes after the onset of the transfusion, a marked difference in the force and volume of the pulse was noted. The blood-pressure rose steadily up to 105 mm. The pulse rate fell with equal steadiness, the respirations became deeper, the collapsed features slowly filled out and color appeared. The symptoms of shock gradually disappeared.

The patient came out of the ether so well, and her condition was so good, that when she was returned to her bed she was placed in a low head-up position (in spite of the treatment of shock requiring a head-down position) to facilitate drainage and keep the mixture of pus and broken-down tissue, carcinomatous and otherwise, from passing upward toward the diaphragm. Large flannel bandages over layers of rough cotton were applied to the extremities. Within a short time she passed 90 c.c. of urine.

The day after the operation there was suppression of urine, and only 30 c.c. were obtained by catheterization. The tube from the abdomen to the vagina drained well. Symptoms of overwhelming infection appeared on the second day, and she died in coma forty-eight hours after the operation. No autopsy was permitted.

Comment.—Had the diagnosis of carcinoma been made before the operation, the latter would not have been attempted, nor would the removal of so large a cyst have been attempted

if the extent and acuteness of the infection had been foreseen. The exposure of so much raw surface would necessarily have led to the absorption of a fatal amount of toxic material, and, as it was, the opinion was held that death was primarily due to this cause. The dissection was carried over every part of the pelvis in eliminating one pathological condition after another as it was found. The removal of the carcinoma was too much of a burden to add to the load already being carried, but once started there could be no retreat. The transfusion satisfactorily overcame the surgical shock, but it was not effective against the toxemia.

The statistics of this case are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Before transfusion.	4 600,000	80%	30,000
After transfusion.	4,800,000	80%	24,000
1st day.	4,928,000	85%	39,680

During the Transfusion

Time	Blood-Pressure	Pulse	Respiration	Remarks
1.15 P.M.	50 mm.	164	30	
1.40 P.M.	65 mm.	144	32	
1.52 P.M.	70 mm.	148	32	
2.00 P.M.	60 mm.	148	34	Began to transfuse.
2.02 P.M.	50 mm.	148	40	
2.05 P.M.	55 mm.	152	40	
2.07 P.M.	75 mm.	150	36	
2.10 P.M.	85 mm.	148	20	
2.18 P.M.	85 mm.	124	28	
2.24 P.M.	90 mm.	140	26	
2.28 P.M.	105 mm.	124	24	
2.31 P.M.	105 mm.	124	24	Stopped transfusing.

Note.—The day after the transfusion the blood-pressure was 95 mm., the pulse 140, and the respirations 26 per minute.

The Donor

Time	Red Count	Hemoglobin	White Count
Before transfusion.	5,280,000	100%	8,000
Immediately after.	4,716,000	90%	12,400
1st day.	5,120,000	90%	9,520

(See Chart, Fig. 16, p. 106.)

Case No. VIII, 5 (6,737). Abstract.

Profound Shock Following Crush of Leg by Train; Temporary Relief after Subcutaneous Saline Infusion; Transfusion Eighteen Hours after Injury; Immediate and Permanent Elimination of Shock; Amputation; Death from Septicemia Seven Days Later.

The patient was a German boy, six years of age, who was run over by a train and his left thigh and leg crushed.

He was admitted to the hospital in a state of profound shock. There was free oozing from the mangled limb. He was at once placed in the head-down position to cause the blood to gravitate toward the heart as much as possible, and was given subcutaneous injections of normal saline solution, but improvement was only temporary. On account of the objections of the parents no surgical measures could be undertaken, and even if permission could have been obtained, the child was at no time in condition for amputation alone. For eighteen hours purely temporizing measures were employed. At the end of that time his pulse was impalpable, the respirations were 60 per minute, and the end was obviously near at hand. Consent finally being obtained, it was decided to endeavor to eliminate the shock by transfusion, and then amputate as quickly as possible. At this time marked infection was present.

The boy's father served as donor. But little difficulty was experienced in anastomosing one of his radial arteries to the median basilic vein of the son by the suture method. After the blood had been allowed to flow across for five minutes the radial pulse appeared again and could be counted. After ten minutes the general condition had markedly improved; the deep lines in the face and the pallor began to disappear. At the end of twenty minutes the lips were pink, there was slight color in the face, ears, and palms of the hands, and he became conscious. The pulse had become fairly good, although it was still rapid, and ranging from 140 to 150. At the

end of thirty minutes it had fallen to 120 and the blood-pressure had risen from 72 to 90 mm.

All preparations had been made to amputate the leg, and the anastomosis was not disturbed during the etherization. The leg was removed as quickly as possible, the circulation being watched carefully while it was being done. No special changes occurred. At the end, as there had been some loss of blood and the amputation had been done close to the hip, a little more blood was allowed to flow across from the father. The patient's face was then full, he was warm, the pulse was 120 and regular, the blood-pressure 95 mm., and the general condition was good. His face was really so florid that it was considered that rather an excessive amount had been transfused, and during the operation it was noticed that the tissues were somewhat overcharged with blood. Fearing the possible occurrence of embarrassment of the right heart, or of the pulmonary circulation, he was placed in a moderate head-up position. Even then his face remained red and full and his condition was good.

After this, no symptoms of shock ever reappeared. Unfortunately, the forced early temporizing permitted very serious infection to develop, and death occurred from septicemia seven days after the transfusion.

Comment.—In spite of the fatal outcome, this case was most encouraging. It was a typical example of severe traumatism followed by profound shock such as usually ends fatally. The shock element was completely eliminated by the transfusion. Death was due to infection.

Case No. VIII, 6 (6,898). Abstract.

Colloid Carcinoma of the Sigmoid Flexure, etc.; Ascites; Removal of Hemorrhagic Fluid; Laparotomy; Removal of as much of the Growth as Possible; Grave Shock; Transfusion; Complete and Permanent Recovery from Shock; No Apparent Effect of Transfusion on Growth; Death Sixty-six Days after Transfusion.

The patient was an American woman, forty-six years of age, who complained of abdominal bloating and pain, and obstruction in her bowels. Her mother had cancer of the face, and two brothers and four sisters were living and well. Her father died at eighty years of age of apoplexy. There was tuberculosis in her husband's family. She had had hemorrhoids for twenty years, which were

removed four weeks previously. Since then she had had slight bleeding. She was always constipated—at times going two weeks without a movement of her bowels. For several years she had been troubled with eructations of gas. At times she had gulped up bile, and her husband said that she had been jaundiced twenty-five years previously. For three or four years she had had frequency of micturition at night, getting up eight to ten times every night.

For the last two or three years her abdomen had been larger than normal, and at times temporarily increased in size. When largest she had generalized pain. The constipation had not increased, she had lost weight for several months, and had had no jaundice or vomiting.

The abdomen was found to be uniformly distended, the flanks bulging equally and smooth and shining. The upper part was tympanitic. Fluid was present in the lower part. No liver dullness was present below the costal margin. No masses could be made out. There was constant pain after palpating the flanks. The ankles were not edematous.

A short incision was made below the umbilicus, a large trochar inserted, and about a liter of hemorrhagic fluid removed. A tumor mass could then be felt in the lower abdomen.

Four days later a median incision was made in the lower part of the abdomen. More hemorrhagic fluid was found. There was a soft muccid and hemorrhagic mass around the sigmoid flexure. This was shelled out with the fingers. It was partly encapsulated. A similar mass which was very hemorrhagic was anterior to the bladder, and another one involved the left broad ligament. These were removed, including the left broad ligament and tube. The bleeding points were tied with catgut. A cigarette drain was left in place. The patient did not endure the operation at all well, and by the time it was finished she was in a grave state of shock. It was therefore thought best to perform a transfusion with the double purpose of overcoming the shock, and possibly influencing the growth of the tumor. The tumor proved to be a colloid carcinoma.

The donor was not related to the patient. One of his radial arteries was anastomosed to a venous branch near the forearm of the patient by the cannula method. The blood was allowed to flow across for twenty minutes.

At the end of the transfusion the patient had become conscious. Her blood-pressure had risen from 78 to 110 mm., and the symptoms of shock disappeared and did not return. Her red count rose from 4,286,000 to 4,640,000, her hemoglobin from 80 to 85 per cent, and

her white count from 19,000 to 42,000. She felt stronger and was soon able to walk about. The wound was drained for fifteen days and then closed. One month after the transfusion her feet became very edematous, and remained so until she was discharged from the hospital. The abdomen refilled with fluid and she complained of pain in her bowels. Two months and six days after the transfusion death occurred.

Comment.—The transfusion was entirely successful in overcoming shock. The effect was both immediate and permanent. The growth of the cancer was unaffected as was to be expected from previous similar experiences.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Before operation.	4,286,000	80%	19,000
After transfusion.	4,640,000	85%	42,000
2d day.	4,416,000	80%	32,000
3d day.	4,400,000	80%	36,000
4th day.	2,696,000	60%	8,400
7th day.	4,160,000	80%	9,600
8th day.	4,000,000	80%	12,040
11th day.	3,940,000	80%	10,000
12th day.	4,280,000	80%	9,000
13th day.	4,360,000	80%	11,000
16th day.	4,300,000	80%	10,000
17th day.	4,204,000	80%	8,000
19th day.	4,180,000	80%	7,040
20th day.	4,140,000	80%	7,000
32d day.	3,900,000	85%	6,200

(See Chart, Fig. 59.)

During the Transfusion

Time	Blood-Pressure	Pulse	Respiration
12.35 P.M.	78 mm.	116	20
12.40 P.M.	78 mm.	120	16
12.43 P.M.	94 mm.	124	16
12.49 P.M.	96 mm.	120	16
12.55 P.M.	110 mm.	120	16
1.00 P.M.	110 mm.	120	16

The Donor

Time	Red Count	Hemoglobin	White Count
Day before transfusion.	4,840,000	100%	7,000
After transfusion.	4,700,000	100%	8,480
7 hours after.	4,160,000	90%	7,440
2d day.	4,100,000	90%	8,040
9th day.	4,900,000	100%	8,040

(See Chart, Fig. 17, p. 108.)

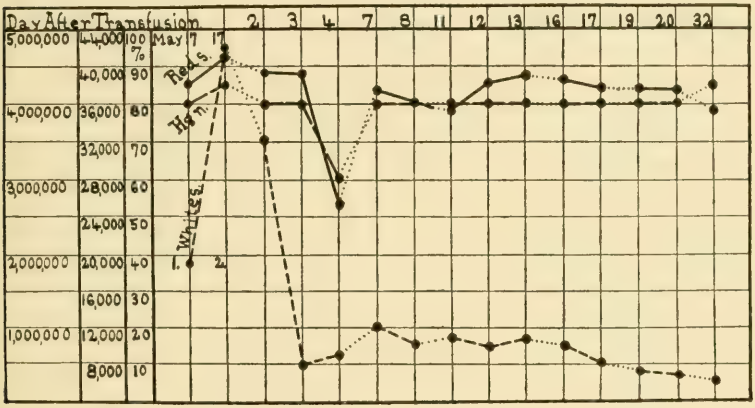


FIG. 59.—CASE NO. VIII, 6 (6,898). BLOOD CHART OF RECIPIENT. COLLOID CARCINOMA OF SIGMOID FLEXURE AND OTHER VISCERA. 1. Just before operation and transfusion. 2. After transfusion. Duration of transfusion, twenty minutes. No explanation could be found for the abrupt fall in the red cells and hemoglobin on the fourth day. No symptoms of hemolysis occurred at this time.

CASE NO. VIII, 7 (6,895). ABSTRACT. CONSULTATION WITH DR. A. H. BOGART AND DR. WOLFE.

Severe Traumatism from Crushing Injury; Profound Shock; Internal Concealed Hemorrhage; Transfusion; Temporary Improvement; Laparotomy by Dr. Bogart; Removal of Torn Spleen and Extravasated Blood; Death in Three and a Half Hours; Retroperitoneal Perirenal Hematoma, Ruptured Renal Vein, and Lacerated Liver Found at Autopsy.

The patient was a boy, eight years of age, who was run over by a truck and brought into the Methodist Episcopal Hospital, Brook-

lyn, N. Y., in a state of profound shock. He complained of severe abdominal pain. The abdomen was distended, and everywhere rigid. Apparently there was fluid in the flanks, as what seemed to be a fluid wave, and dullness which was somewhat movable, were present. Nothing abnormal was found in the chest. There was marked dilatation of the superficial veins of the upper part of the body. After consultation with Dr. Bogart it was decided that immediate transfusion offered the greatest hope of recovery if the shock could be overcome enough by it to warrant an exploratory operation.

The donor was the patient's mother. One of her radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for twenty-six minutes.

During the first eighteen minutes of the transfusion the pulse fell from 140 to 110 per minute, and improved in volume and force. The respirations were unaffected. During the next eight minutes the pulse began to rise again, became of poorer quality, and the color of the face and the general condition, which had improved, again became poor. Dr. Bogart then very quickly and skillfully performed a laparotomy, excising the lacerated spleen and washing out the blood found in the abdomen. The shock was somewhat increased. The patient lived three and a half hours longer, and then respiratory failure occurred.

The postmortem examination made through the laparotomy wound revealed an extensive retroperitoneal hematoma around the left kidney, a rupture of the left renal vein, and several small lacerations of the liver. The spleen was nearly torn in two. No examination of the thoracic organs was made.

Comment.—In this case the crushing force which caused the traumatism extended across the middle of the trunk, involving the lower thorax as well as the upper abdomen. The enlarged veins, the very marked respiratory disturbance, and a certain irregularity of the cardiac rhythm brought strongly to mind phenomena observed in experimental work with direct traumatism of the heart. While watching the pulse after the transfusion and noticing the decline in volume and tension, it was strongly felt that there was either a cardiac lesion or some undetermined action still continuing. The post-mortem ex-

amination showed that the hemorrhage had continued after the operation, but permission could not be obtained to examine the chest to determine whether or not the suspicion as to injury of the heart was well founded.

Case No. VIII, 8 (7,109). Abstract. Consultation with Dr. J. M. Waugh.

Tuberculous Abscess in True Pelvis; Laparotomy; Partial Removal of Adhesions; Insertion of Cigarette Drains; Patient in Profound Shock at End of Operation; Transfusion; Disappearance of Symptoms of Shock; Uneventful Recovery; Patient Well After Elapse of More than Twelve Months.

The patient was an American woman, twenty-six years of age, with negative family history. Her general health had been good, her menstruation normal, and she had had no discharge from the vagina. She complained of having an uncomfortable feeling in her abdomen.

Six weeks before entering the hospital she had had tonsillitis. She felt better at the end of two days, then had high fever, and had been in bed ever since with fluctuating fever and night sweats. The entire abdomen began to be painful two weeks after she went to bed. She had no pain going down her legs or into her back. Since the illness began she had had occasional burning on urinating, but no frequency.

The physical examination showed the patient to be emaciated. The expansion of the chest over the right upper part was limited, and this area was flattened. Above the clavicle there was dullness on percussion. The expiration was much prolonged. The heart sounds were clear and of good quality. The abdomen was full, and tympanitic in the flanks. In the right lower quadrant there was a mass 6 by 8 cm. between the symphysis pubis and the anterior superior spine of the ilium. It was dull on percussion and tender on palpation.

At the operation an incision 10 cm. long was made in the median line below the umbilicus. The Fallopian tubes were found to be matted down in the pelvis and covered with dense adhesions. On pulling the uterus forward an abscess in the posterior *cul-de-sac* was ruptured and the pus escaped. The adhesions were partially broken up, cigarette drains were inserted, and the abdominal wound partly closed.

As the patient was in a condition of profound shock when the operation was completed, it was decided to transfuse. A sister of the patient served as donor. One of her radial arteries was anastomosed to a median basilic vein of the patient near the elbow by the cannula method. The blood was allowed to flow across for thirty-five minutes.

By the end of the transfusion the patient's blood-pressure had risen and her pulse rate fallen. Her face was ruddy and she showed no signs of shock. She was taken to the ward and placed in the head-up position. The transfusion was entirely uneventful, as well as her subsequent recovery from the operation. The pathologist reported that the pelvic abscess was of tuberculous origin.

After more than twelve months had elapsed the patient was well, having gained 38 pounds in weight.

Comment.—Transfusion well served its purpose in this case in eliminating the shock factor. The patient made an unexpectedly rapid and complete recovery. At present there are no signs of tuberculosis.

Case No. VIII, 9 (7,476). Abstract. Consultation with Dr. C. W. Thomas, Warren, Ohio.

Localized Multiple Hematogenous Infection of Kidney; Patient in Poor Condition; Transfusion to Prevent Postoperative Shock; Nephrotomy; Excision of Infected Area; Operation Borne Well without Appearance of Shock; Long and Stormy Convalescence; Recovery.

The patient was an American woman, forty-one years of age, who complained of having pain in her right side. Her family had no history of tuberculosis, neoplasm, or hemophilia. She had had diphtheria, the usual diseases of childhood, and typhoid fever eighteen years previously.

The patient had been ill for about two months. Her symptoms were those of a chronic infection characterized by wide variations in temperature, occasional chills, profuse sweating, emaciation, and loss of strength. It was supposed that she had tuberculosis of the kidney, complicated with a pyogenic infection, but careful search failed to reveal tubercle bacilli. An X-ray examination was negative as regards renal calculus or pyelitis. Catheterization of the ureters

showed markedly diminished urinary secretion from the right kidney, while that from the left was normal. The urine contained some leucocytes and an occasional red corpuscle. In the absence of evidence of calculus, specific infection, ascending infection from the bladder, and with symptoms too severe for a tuberculous process, the diagnosis of probable multiple hematogenous infection of the renal parenchyma was made.

The patient's general condition was very poor. Her red count was 2,320,000, hemoglobin 30 per cent, and her white count 13,500. Her pulse and temperature varied extremely, and she was obviously such a poor surgical risk that it would have been unwise to have attempted an extensive operation on the kidney without transfusion.

The transfusion was first performed in the usual way, the flow lasting thirty-eight minutes. Then the patient was anesthetized, and the kidney exposed and bisected. Inspection of the cut surface revealed nothing. The organ was large, vascular, and soft. Finally, after careful search, an area containing a small necrotic focus was found. As it was apparently present in this place alone, the portion of the kidney containing it was excised and the kidney packed and replaced with drainage inserted in the external wound. The subsequent microscopical examination showed it to be a multiple hematogenous infection. The patient bore the operation well, and after a rather long and stormy convalescence made a good recovery.

Comment.—Operation in this case was rendered safe by transfusion. The shock factor was eliminated.

SUMMARY

Case No. VIII, 1 (6,695).

Transfused.—For postoperative collapse (actinomycosis in the true pelvis).

Immediate Result.—Complete resuscitation; patient improved.

Other Treatment.—Vaginal puncture; establishment of drainage.

Late Result.—Death four weeks after transfusion.

Case No. VIII, 2 (7,122).

Transfused.—For postoperative collapse of cardiac origin (panhysterectomy for sarcoma of uterus and ovaries, complicated with pyogenic infection).

Immediate Result.—Death in a short time.

Case No. VIII, 3 (7,123).

Transfused.—For shock following complete avulsion of arm.

Immediate Result.—Entire disappearance of shock.

Other Treatment.—Disarticulation of stump of humerus, 1,000 c.c. of saline infusion given before the transfusion without lasting benefit.

Late Result.—Uninterrupted recovery.

Case No. VIII, 4 (6,849).

Transfused.—For shock following panhysterectomy (carcinoma of uterus and sigmoid flexure, infected bilateral multilocular broad ligament cysts).

Immediate Result.—Elimination of symptoms of shock.

Other Treatment.—Postural drainage, bandaging of extremities.

Late Result.—Death from toxemia on second day after transfusion.

Case No. VIII, 5 (6,737).

Transfused.—For profound shock following crush of leg by train.

Immediate Result.—Complete elimination of shock.

Other Treatment.—Previously given saline infusion (which was of temporary benefit only), amputation of leg (the transfusion was both before and after the amputation).

Late Result.—Death from infection at end of seven days.

CASE No. VIII, 6 (6,898).

Transfused.—For shock after laparotomy for colloid carcinoma.

Immediate Result.—Complete elimination of shock.

Other Treatment.—None for elimination of shock.

Late Result.—Death from carcinoma sixty-six days after transfusion.

CASE No. VIII, 7 (6,895).

Transfused.—For shock and internal hemorrhage following crushing injury.

Immediate Result.—Temporary improvement only.

Other Treatment.—Laparotomy, splenectomy.

Late Result.—Death in three and a half hours (renal vein found to be ruptured).

CASE No. VIII, 8 (7,109).

Transfused.—For shock following laparotomy for tuberculous abscess in true pelvis.

Immediate Result.—Elimination of shock.

Other Treatment.—Partial freeing of adhesions to evacuate pus, insertion of drains.

Late Result.—No return of shock, uninterrupted convalescence, effect on tuberculous process to be determined.

CASE No. VIII, 9 (7,476).

Transfused.—To prevent shock after nephrotomy for multiple infection of kidney.

Immediate Result.—No shock developed.

Other Treatment.—None.

Late Result.—Recovery.

CASE FROM ANOTHER SOURCE

Case A. Mumford and Greenough.[1]

Appendectomy following Perforating Appendicitis; Acute Intestinal Obstruction; Operation and Resection of Ten Inches of Intestine; Secondary Lateral Anastomosis; Shock and Hemorrhage; Transfusion; Improvement; Recovery.

The patient was a male, thirteen years of age (Mass. Gen'l Hosp., No. 157,024). "Operated on February 13, 1908, twenty-four hours after onset of symptoms. Appendix perforated. Drained.

"February 20th. Severe abdominal pain.

"February 21st. Operation for acute intestinal obstruction and resection of ten inches of intestine.

"April 1st. Secondary lateral anastomosis, after which there was much pain and restlessness, and a steadily progressing weakness of pulse.

"April 2d. Patient in very poor shape, and transfusion done by Drs. Mumford and Greenough under cocain. The left radial artery of the donor and one of the brachial veins of the patient were united, but no blood seemed to pass. A new connection was made in thirty minutes. This remained for thirty minutes with good results. During the afternoon the pulse became slower and better and the patient improved. This improvement steadily continued.

"May 4th. Patient discharged well to local doctor."

CONCLUSIONS

Anemia plays an important rôle in the cause of death from shock. If there is sufficient blood in the vascular system as a whole the circulation through the central nervous system is efficient. Therefore transfusion is a valuable treatment for uncomplicated shock.

---

[1] The account of this case was received in a personal communication from Dr. R. B. Greenough, of Boston, Mass.

CHAPTER XXV

HEMORRHAGE

(*Group IX*)

CASE NO. IX, I (6,411). ABSTRACT. CONSULTATION WITH DR. W. G. STERN.

Nephrolithiasis; Nephrotomy; Intractable Postoperative Hemorrhage into the Wound and into the Bladder; Prostration of Patient; First Transfusion; Revival of Patient; Nephrectomy; Suprapubic Cystotomy for Removal of Blood Clots from Infected Bladder; Severe Cystitis; Suppression of Urine; Uremia; Improvement for Two Weeks; Severe Continuous Hemorrhage from Bladder Wall; Second Transfusion; Complete Cessation of Hemorrhage; Recovery; No Return of Hemorrhage in Twenty Months.

The patient was a Russian, twenty-three years of age, with entirely negative family and personal history as far as the illness under discussion is concerned.

Three years previously he had had an attack similar to the one for which he entered the hospital. Three months previously he was examined for life insurance, and his application rejected after his urine was examined. At this time he felt pretty well, but he had occasional twinges of pain in his left side. His condition remained about the same up to the time of operation. The diagnosis of renal calculus was made.

The left kidney was exposed by an oblique lumbar incision, and found to be well up under the costal arch and adherent to the peritoneum. It was enlarged, especially in its long axis, and extremely vascular. It was found necessary to divide the twelfth rib in order to deliver it.

After considerable difficulty the kidney was displaced outward sufficiently to make it possible to control the blood supply and make room for the incision. The capsule was normal in appearance, but of increased vascularity. A 4-cm. mid-pole longitudinal incision was made, and a large stone found occupying the pelvis and all the calices. This was carefully removed in several pieces, sparing the

kidney as much trauma as possible while doing so. The granulation tissue in which the stone was embedded bled very freely on extracting it. Pressure on the renal artery controlled the bleeding promptly. After a careful exploration of all the calices and the upper ureter, the wound was snugly packed with gauze. This also controlled the bleeding. As the calices were infected, the external wound was only partially closed by means of sutures and the remainder was packed. The patient left the table in good condition, although a considerable amount of blood was lost altogether.

In the first twenty-four hours after the operation there was only a slight amount of oozing from the dressings, but there was a rather unusual amount of discoloration of the urine. On the second day the patient's condition seemed to be favorable. There was still some oozing. On the third and fourth days the hematuria was markedly increased in spite of all the measures which were undertaken to prevent it.

On the morning of the fifth day the situation had grown more critical, and Dr. Lower removed all the packing in order to obtain a more effective hemostasis. While he did this there was a very profuse hemorrhage, apparently from the tissues and granulations and not from a large vessel or vessels. After this the hemorrhage was almost equally profuse both through the dressings and the ureter. The bladder was filled with blood, which was voided as a full stream of almost pure blood. The patient's condition had become very critical, so that considerable anxiety was felt as to the outcome. During the day the endeavor was made to overcome the effects of the loss of blood which had already occurred, and to prevent further loss by the use of pressure, inclined posture, bandaging the extremities and the abdomen up to the costal borders, repeated saline infusions, heat, and different stimulants and other internal medication. In spite of these measures he steadily sank, and the oozing continued until the end of the afternoon. It was then obvious that death was near unless some means of relief could be obtained. The red blood count at 4 P.M. was 1,800,000, and the hemoglobin 40 per cent. The blood-pressure was 68 mm., and the pulse rose from 106 to 155, and then to 170 beats per minute, the respirations were shallow, and the extremities were cold.

A radial artery of one of the patient's brothers was anastomosed to a median basilic vein of the patient by the suture method by the usual technic. The blood was allowed to flow across for twenty minutes.

The blood-pressure of the patient gradually rose from 68 to 94 mm., the pulse fell from 160 to 120, the respirations fell from 48 to 28 per minute and became deeper and more regular. The red count rose from 1,800,000 to 2,600,000, and the hemoglobin from 40 to 50

per cent. The most striking change, however, was in the general condition. The cold, clammy, ghastly, yellowish complexion gradually changed to a more normal one. The orbital spaces gradually filled out, and the lips and ears became tinged with pink. The changes were exactly similar to those which occur when a person comes out of a faint.

At the end of twenty minutes the improvement was so great that it was thought safe to stop the transfusion and perform a nephrectomy in order to attack the bleeding at its source. Under ether anesthesia the patient's lumbar wound was reopened with a gush of blood coming out as soon as the packing was removed. The swelling of the surrounding parts made it necessary to enlarge the opening. After very considerable difficulty the kidney was delivered, the vessels were tied, and the kidney cut away. The difficulty of the operation subjected the patient to considerable shock, but he bore it very well. He was at once put into the pneumatic suit and his blood-pressure sustained for several hours. Afterwards his extremities and lower abdomen were bandaged with several layers of coarse cotton with three or four layers of heavy cotton flannel outside. The bed was elevated and normal saline solution was given by rectum.

The patient rallied well after the operation and passed the night safely. The next morning the bladder was found to be overdistended with urine and clotted blood from the previous hemorrhages. He was catheterized after the operation the evening before, but in the urgency of the situation the clot was not noticed. Under cocain anesthesia during continuous subcutaneous saline infusion in the head-down posture on the operating table, the bladder was quickly opened and a large amount of ammoniacal urine mixed with blood clot was evacuated. The bandages were then once more applied from the toes to the costal borders, and he was kept in the same posture under perfect quiet. Hot applications were applied over the remaining kidney.

Following this, acute suppression of the urine occurred, and uremia twelve hours later. Vigorous counterirritation and the use of potassium acetate and digitalin were followed by renewed activity of the remaining kidney, which secreted 36 ounces in the next twenty-four hours.

During the next two weeks there was no hemorrhage, the wound in the loin was more than half healed, and the suprapubic wound was partially healed in spite of the persistence of the severe cystitis. Suddenly there occurred a considerable hemorrhage from the bladder wall without the least warning preceding it. It continued for

forty-eight hours, and showed no signs of stopping in spite of the intravesical injection of large amounts of adrenalin, the application of ice bags to the lower abdomen, and various other measures.

By the fortieth hour after the bleeding began, the red count had fallen to 1,800,000, the hemoglobin to 23 per cent, and the oozing still continued. A second brother of the patient then offered to act as donor, and one of his radial arteries was anastomosed to a venous branch near the elbow of the patient by the suture method as before. The blood was allowed to pass over for twenty-eight minutes in all, with interruptions as occasion demanded.

During the transfusion the patient complained of precordial distress, and loudly proclaimed that he felt sick. His respiratory rate was markedly increased. Later he was seized with a chill, accompanied by considerable circulatory disturbance. The immediate improvement was marked, although not so great as at the last time. After he was put back to bed he regained his composure. A marked improvement had occurred in the blood count and hemoglobin, and the general symptoms were improved. Although no more treatment of any sort was

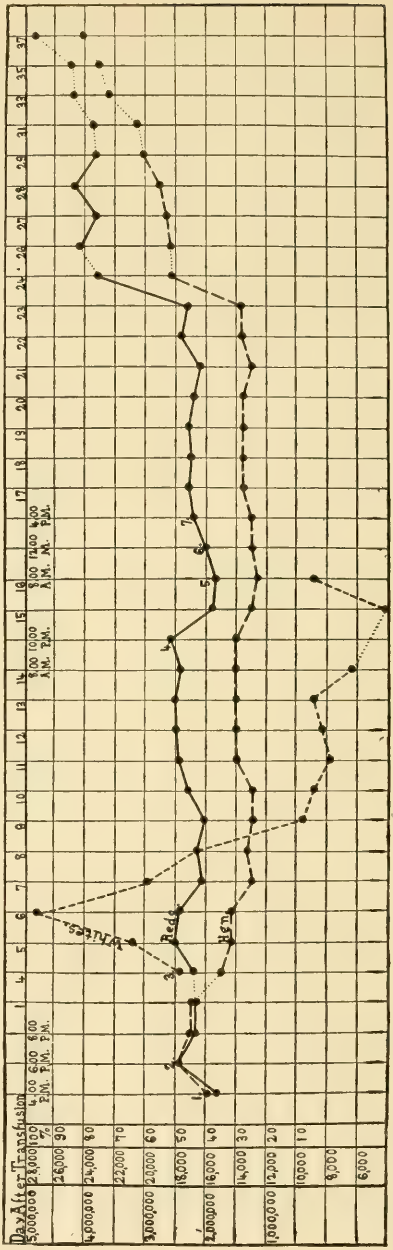


FIG. 60.—CASE NO. IX, 1 (6,411). BLOOD CHART OF RECIPIENT. NEPHROLITHIASIS, POST-OPERATIVE HEMORRHAGES. 1. Before first transfusion. 2. After first transfusion. 3. Severe cystitis. 4. Hemorrhage from bladder wall. 5, 6, 7. Before, at beginning of, and after second transfusion. Duration of first transfusion, twenty minutes; of second transfusion, twenty-eight minutes.

given, the bleeding ceased after several hours and never returned. The wounds all improved rapidly, the granulation tissue became red and active, and healing quickly followed.

The patient was soon able to assume his previous work. At the present time, twenty months after the second transfusion, he is in good health. His present red count is 6,500,000, and his hemoglobin 100 per cent.

Comment.—This case demonstrates the specificity of transfusion in the treatment of acute hemorrhage, and a probable effect on pathologic hemorrhage.

THE RECIPIENT

First Transfusion

TIME	Red Count	Hemoglobin	White Count	Remarks
4.00 P.M.	1,880,000	40%	. . . . . .	Just before transfusion.
6.00 P.M.	2,500,000	50%	. . . . . .	Shortly after transfusion and nephrectomy.
8.00 P.M.	2,200,000	45%	. . . . . .	
1st day.				
5.00 P.M.	2,200,000	45%	. . . . . .	
4th day.	2,236,000	35%	17,800	Patient had severe cystitis.
5th day.	2,540,000	32%	21,000	Polymorphonuclear leucocytes, 90%.
6th day.	2,490,000	32%	27,400	
7th day.	2,100,000	25%	20,000	Many macrocytes and microcytes, some poikilocytosis, no nucleated red cells.
8th day.	2,180,000	27%	16,800	
9th day.	2,040,000	25%	9,600	
10th day.	2,310,000	25%	8,800	
11th day.	2,460,000	30%	7,800	
12th day.	2,500,000	30%	8,400	Condition of blood improved.
13th day.	2,510,000	30%	9,000	
14th day.				
8.00 A.M.	2,420,000	31%	6,400	
10.00 P.M.	2,600,000	31%	. . . . . .	Severe hemorrhage from bladder.
15th day.	1,900,000	25%	4,000	Patient's condition much worse. Coagulation time of blood, six and a quarter minutes.
16th day.	. . . .	. . . .	. . . . . .	Coagulation time, four minutes.
8.00 A.M.	1,860,000	23%	8,800	

THE RECIPIENT—*Continued*

Second Transfusion

Time	Red Count	Hemoglobin	White Count	Remarks
12.00 M.	2,000,000	25%	......	Transfusion began at 12.16 P.M.
4.00 P.M.	2,256,000	25%	......	
17th day.	2,264,000	28%	8,000	Coagulation time, five and three quarter minutes. Considerable poikilocytosis.
18th day.	2,229,000	28%	......	
19th day.	2,220,000	28%	......	
20th day.	2,100,000	25%	9,800	
21st day.	2,414,000	30%	......	
22d day.	2,324,000	30%	......	
23d day.	3,696,000	50%	......	
26th day.	4,072,000	52%	......	Condition of blood improving.
27th day.	3,832,000	55%	6,600	
28th day.	4,160,000	55%	......	
29th day.	3,816,000	60%	......	
31st day.	3,856,000	62%	......	
33d day.	4,176,000	72%	8,400	Very slight poikilocytosis. Very few microcytes.
35th day.	4,200,000	75%	......	
37th day.	4,800,000	80%	......	

(See Chart, Fig. 60.)

CHANGES OCCURRING DURING THE TRANSFUSIONS

First Transfusion

TIME	Blood-Pressure	Pulse Rate	Remarks
4.30 P.M.	68 mm.	150	Pulse of small volume.
5.22 P.M.	75 mm.	...	Began to transfuse.
5.25 P.M.	85 mm.	...	
5.27 P.M.	....	142	Volume better.
5.28 P.M.	90 mm.	...	
5.30 P.M.	....	...	Pulse much improved in every way.
5.32 P.M.	90 mm.	...	
5.34 P.M.	89 mm.	...	
5.36 P.M.	91 mm.	...	
5.38 P.M.	91 mm.	126	
5.40 P.M.	90 mm.	...	
5.43 P.M.	87 mm.	...	
5.44 P.M.	94 mm.	128	

THE RECIPIENT—*Continued*

CHANGES OCCURRING DURING THE TRANSFUSIONS

Second Transfusion

Time	Blood-Pressure	Pulse Rate	Remarks
11.30 A.M.	....	128	Tension low, and volume small.
12.16 P.M.	....	132	Began to transfuse.
12.23 P.M.	....	130	
12.29 P.M.	....	124	
12.35 P.M.	....	116	
12.44 P.M.	....	113	
12.50 P.M.	....	114	
12.58 P.M.	....	118	
1.03 P.M.	....	126	
1.06 P.M.	....	126	Good tension and volume. Stopped transfusing.

THE FIRST DONOR

TIME	Red Count	Hemoglobin	White Count	Remarks
4.00 P.M.	5,000,000	100%	.....	Before transfusion.
6.00 P.M.	3,200,000	70%	.....	After transfusion.
1st day.	3,950,000	75%	.....	
4th day.	4,280,000	80%	9,600	
5th day.	5,250,000	90%	7,800	
6th day.	5,216,000	95%	8,000	
8th day.	5,848,000	100%	8,800	
14th day.	4,750,000	90%	6,000	

(See Chart, Fig. 18, p. 110.)

The Pulse and Blood-pressure During Transfusion

TIME	Pulse	Blood-Pressure	Remarks
4.30 P.M.	76	97 mm.	Before transfusion.
5.22 P.M.	72	....	Began to transfuse.
5.34 P.M.	76	....	
5.36 P.M.	76	....	
5.38 P.M.	80	....	
5.40 P.M.	80	....	
5.42 P.M.	76	....	
5.44 P.M.	76	....	
5.46 P.M.	84	....	
5.48 P.M.	84	....	
5.49 P.M.	87	....	Pulse of good volume.
6.00 P.M.	..	70 mm.	

THE SECOND DONOR

Time	Red Count	Hemoglobin	White Count	Remarks
12.00 M.	7,040,000	100%	7,800	Before transfusion.
1.00 P.M.	5,500,000	90%	.....	After transfusion.
4.00 P.M.	4,844,000	85%	.....	
1st day.	4,800,000	90%	9,400	
2d day.	5,500,000	95%	10,200	
13th day.	7,072,000	100%	.....	

(See Chart, Fig. 19, p. 112.)

The Pulse Rate During Transfusion

Time	Pulse	Remarks
12.00 M.	94	Before the transfusion.
12.16 P.M.	102	During the transfusion.
12.20 P.M.	108	
12.30 P.M.	110	
12.39 P.M.	114	
12.50 P.M.	106	
12.59 P.M.	110	
1.06 P.M.	110	The volume and tension were good.

CASE NO. IX, 2 (6,852). ABSTRACT.

Severe Hemorrhage from Uterus; Prostration of Patient; Transfusion; Revival; Curettage; Discovery of Adenocarcinoma; Immediate Panhysterectomy; Recovery; No Known Recurrence of Growth in Twelve Months.

The patient was an American woman, thirty-eight years of age, and unmarried. Her mother died of heart disease and a brother of tuberculosis. There was no history of neoplasm or hemophilia. Except for the fact that she was curetted for leucorrhea eight years previously, her history was negative.

One year previously she was curetted again, and an ovarian cyst and a submucous fibroid removed at the same time. There was no bloody discharge from the vagina until four months previously, when a slight one began. This gradually increased until five weeks previously, when she had a severe hemorrhage and had been bleeding ever since. She had had no pain or fever but was quite weak.

She was sent to the hospital on account of the intractable nature of the hemorrhage. It was hoped that the use of hot douches, packing, and rest would give relief and opportunity to recover sufficiently from the anemia to warrant anesthesia and the carrying out of the necessary surgical procedures. The first night in the hospital, however, the hemorrhage became profuse, and persisted in spite of intrauterine packing and other measures. It became necessary to resort to subcutaneous saline infusion, and by giving over 1,000 c.c. she was tided over until morning, when she was in very poor condition. At this time the bleeding was progressive, the pulse scarcely perceptible, and she was not an acceptable surgical risk. It was decided to perform a transfusion and then curette her.

A brother of the patient served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for twenty-four minutes.

The immediate effect of the transfusion was most gratifying, the marked symptoms of hemorrhage all disappearing. Her face became full, the lips pink, the pulse of large volume and slower rate, and the respirations less frequent.

All the preparations for operation had been made. It was not suspected at this time that there was a malignant growth, but rather that there was a recurrence of the submucous fibroid removed at the operation a year previously. The curettage was begun, and it was at once found that carcinoma of the fundus was present. A panhysterectomy was immediately done as rapidly as possible. The patient endured the operation well, and came out of the anesthetic in good condition.

After the operation her pulse was rather rapid, but her condition remained good, the blood-pressure being slightly subnormal and the face full. On the third day there was a considerable drop in the red count and hemoglobin, which was unaccompanied by the presence of blood pigment in the urine, or anything else which suggested hemolysis. The loss was soon made up, and she made an excellent recovery. Up to the present time, twelve months after the operation, her health has been good and there has been no discoverable sign of recurrence. The pathologist reported the case to be an adenocarcinoma.

Comment.—In this instance transfusion was plainly a life-saving procedure, as every means at command failed to arrest

the hemorrhage and bring the patient out of her critical condition. Without transfusion the panhysterectomy could not have been successfully performed.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count
Evening before.	3,872,000	75%	8,080
Before transfusion.	3,800,000	70%	10,040
After transfusion and operation.	3,340,000	70%	9,000
1st day.	2,480,000	70%	10,040
4th day.	1,920,000	50%	8,040
5th day.	2,520,000	70%	7,000
8th day.	3,520,000	70%	8,880
9th day.	3,680,000	70%	7,000
11th day.	3,200,000	70%	8,000
12th day.	3,840,000	70%	7,040
13th day.	3,264,000	....	......
15th day.	3,360,000	70%	8,000
18th day.	3,580,000	70%	6,040
19th day.	3,840,000	80%	6,000
20th day.	3,780,000	80%	7,040

(See Chart, Fig. 61.)

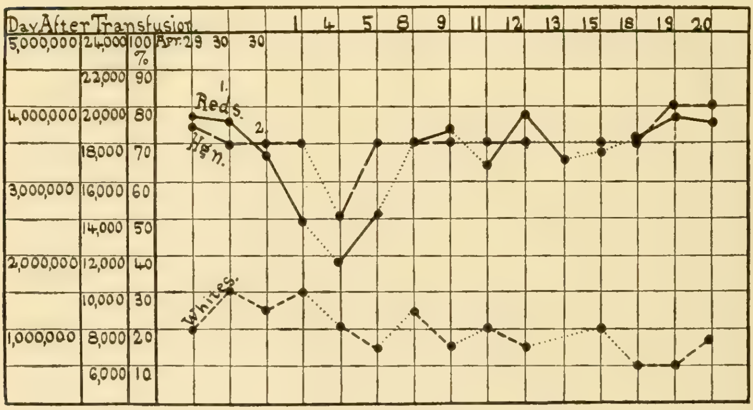


FIG. 61.—CASE NO. IX, 2 (6,852). BLOOD CHART OF RECIPIENT. ADENOCARCINOMA OF UTERUS, ACUTE HEMORRHAGE. 1, 2. Just before transfusion, and just after transfusion and operation. Duration of transfusion, twenty-four minutes.

During the Transfusion

Time	Blood-Pressure	Pulse	Respiration
9.25 A.M.	110 mm.	144	20
9.32 A.M.	120 mm.	136	20
9.44 A.M.	120 mm.	148	18
9.46 A.M.	120 mm.	134	16
9.53 A.M.	120 mm.	136	16

Case No. IX, 3 (7,110). Abstract.

Appendicitis; Appendectomy; Closure of Abdominal Wound; Twelve Hours Later Severe Attack of Vomiting Followed by Internal Concealed Hemorrhage from Mesoappendiceal Artery; Incision through Right Rectus Muscle; Removal of about 1,500 c.c. of Clotted Blood from Abdomen; Religation of Spurting Mesoappendiceal Artery; Transfusion; Marked Improvement with Removal of Effects of Hemorrhage; Return to Ward in Good Condition; Accumulation of Gas in Stomach; Passage of Stomach Tube; Violent Retching with Tearing of All but Skin Sutures in Incision through Rectus; Skin Sutures Removed; Abdomen Reflushed; Drain Inserted; Continued High Temperature; Death Apparently from Bacteriemia on Morning of Third Day.

The patient was an American, twenty-six years of age, who was operated on by a surgical colleague. His family history was negative. He had had the usual diseases of childhood, and typhoid fever three years previously. He complained of pain in his right lower abdomen.

Two weeks before entering the hospital he had had soreness in the same region. The physical examination was negative except that there was tenderness over the appendix on deep pressure. No mass could be felt.

At the operation the abdomen was opened by a 10-cm. McBurney incision. The appendix was found to be congested but not adherent. The mesoappendix was freed from the appendix and carefully ligated with catgut. The appendix was then ligated, removed, and the stump inverted and held in place with a purse-string suture. The denuded surface of the mesoappendix was covered with peritoneum. The abdominal wound was closed in layers with catgut, chromic catgut, and horsehair. The patient stood the operation well. When returned to the ward he was propped up in bed. Twelve hours later he had a severe attack of vomiting,

and it was probably at this time that the ligature on the meso-appendiceal artery was torn off.

At 10.25 P.M. he was perspiring. His pulse was 128 per minute. At 11.00 he was perspiring profusely, his pulse had gone up to 140 and was running with small volume and low tension, and there was movable dullness in the flanks. A diastolic murmur had developed in the heart. At 11.20 his condition was considerably better. At 6.30 the next morning he had Cheyne-Stokes respiration, his pulse was 140 and poor in character. He had been kept quiet during the night with morphin, and had had ice-bags on his abdomen. The diagnosis of internal hemorrhage was made, and transfusion and laparotomy were decided to be the best means of treatment.

A brother of the patient served as donor. One of his radial arteries was anastomosed to a superficial vein of the patient near the elbow by the cannula method, the vein being cuffed back and the artery placed over it. The blood was allowed to flow across for thirty-one minutes, but not uninterruptedly, as the stream was partly stopped during the laparotomy.

The abdomen was reopened by a 15-cm. incision in the right rectus muscle and found to be filled with partly clotted blood, the amount being estimated at 1,500 c.c. The mesoappendiceal artery was found to be spurting, and therefore the source of the hemorrhage. The whole abdomen was flushed out with normal saline solution until it was clear. The wound was closed in the usual way with catgut in the peritoneum and muscles, chromic catgut in the fascia, and horsehair in the skin.

As a result of the transfusion the blood-pressure of the patient rose from 75 to 105 mm. of mercury, the pulse fell from 140 to 126 beats per minute, and the respirations fell from 28 to 26 per minute. The general condition was very much improved—in fact, the symptoms of acute hemorrhage were practically eliminated.

At 5.30 that afternoon the patient was so much troubled by gas in the stomach that a tube was introduced to give relief. This brought about intense retching, which in turn caused the incision in the right rectus to break open underneath the skin. On removing the patient to the operating room and cutting the skin sutures, the intestines welled up into the wound, all the fascia and muscle sutures having parted or been torn out. The peritoneal coating on a loop of ileum which presented was ruptured for a distance of 7 cm. This was repaired with linen and the peritoneal cavity again flushed out with saline solution. Some blood from the previous hemorrhage came away from under the diaphragm, which had not

been washed out before. (During the first hemorrhage the patient had been placed in the head-down position, so that the remaining intravascular blood would gravitate toward the heart, which, of course, prevented the blood in the cavity near the diaphragm from descending as it would otherwise have done.) There was only slight local peritonitis present, but no more fresh blood, showing that the second ligature of the mesoappendiceal artery had held. The wound was not sewed up entirely and drainage was inserted. When the patient was returned to the ward his rectal temperature had gone up to 105° F. He was again propped up in bed in the head-up position on account of the local peritonitis. In spite of all the mishaps, his condition was much improved.

The day after the transfusion the temperature had fallen to 102°, the pulse was 140 and of good volume. Later in the day the abdomen was distended and the respirations were up to 30. The pulse was about the same. Observations at 5 and 9.30 P.M. showed a rise in the white corpuscles from 14,000 to 19,000, the red corpuscles remaining at 4,800,000. The patient was somewhat delirious. At this time the blood cultures showed Staphylococcus pyogenes aureus. This fully accounted for a part of the clinical symptoms which were unexplained before.

By the second day after the transfusion the pulse and temperature were about the same. The patient had had a fairly good night. Constant rectal irrigation with saline solution had been maintained. In the afternoon cathartic enemata with abdominal massage caused active passage of gas by rectum. The hands were cold and clammy and the pulse was not so good. Mild delirium reappeared, which was controlled with morphin. The abdomen was tender, but not rigid. The patient gradually became weaker and died at 3.15 A.M. the next morning. Before death there was no sign of jaundice, and no hemoglobin was found in the urine.

At the autopsy the heart and lungs were found to be in normal condition. Between the liver and diaphragm there was an old blood clot. The luster of the peritoneum was dulled, but there was no definite peritonitis except slight ulceration around the right rectus incision. The liver showed fatty degeneration, and the kidneys chronic interstitial nephritis. The skin was jaundiced. A culture taken from the peritoneal cavity at the time of the second operation —i. e., when the hemorrhage was controlled—revealed colon bacilli. A similar culture made at the autopsy revealed colon bacilli and a growth of Staphylococcus pyogenes aureus.

The appendix was 7.5 cm. long and 0.8 cm. in diameter. The

peritoneal surface was slightly injected. Along the mesenteric side there was considerable, apparently normal fat. The wall was thickened and congested. On the inside there was some fecal matter, but no pus. There was no perforation. About 2 cm. from the proximal end there was a small necrotic area in the mucosa, while the remainder of the mucosa was congested. The histological examination showed that the inflammatory process had extended deep into the muscular coats, and that there had been previous attacks as revealed by the presence of deposits of fibrous tissue occurring in many places.

Comment.—The question at once arises as to what was the cause of death in this case. Shock can be eliminated, as the blood-pressure was 115 mm. the night before death and had been maintained at a safe level. The blood counts showed no destruction of the red corpuscles, no blood pigment was ever present in the urine, and the postmortem icterus could have been due to the absorption of the old blood not removed from the abdomen. Some peritonitis of very mild degree was found at the autopsy, and the presence of colon bacilli was demonstrated. While the hemorrhage following the original operation was severe, its effects were apparently overcome by the transfusion. Bacteriemia seems the most likely explanation. Since the temperature began to rise immediately after the removal of the appendix, and did not fall even during or after the severe hemorrhage, it is probable that the blood infection occurred early, and, as previously stated, staphylococci were found in the blood during life.

Case No. IX, 4 (6,492). Abstract. Consultation with Dr. J. V. Kofron.

Typhoid Fever; Intestinal Hemorrhages; Severe Laryngeal Symptoms; Temporary Improvement; Severe Hemorrhage; Transfusion from Immune Donor; General Improvement; More Hemorrhages; Double Parotitis; Death on the Seventh Day after Transfusion.

The patient was an Italian, twenty-two years of age, with a negative family history. From his personal history it was learned that he

had raised blood on two occasions five or six years previously. He had had night sweats and had coughed a good deal. At times he had shortness of breath and palpitation of the heart. He used tobacco, and drank beer, whisky, tea, and coffee. He denied venereal disease.

His complaint was soreness of the abdomen and general weakness, which he had had for two weeks. The characteristic symptoms of typhoid fever developed with severe bronchial and laryngeal symptoms, and on the twelfth day after he entered the hospital he had two small hemorrhages from the bowels. In the next two days

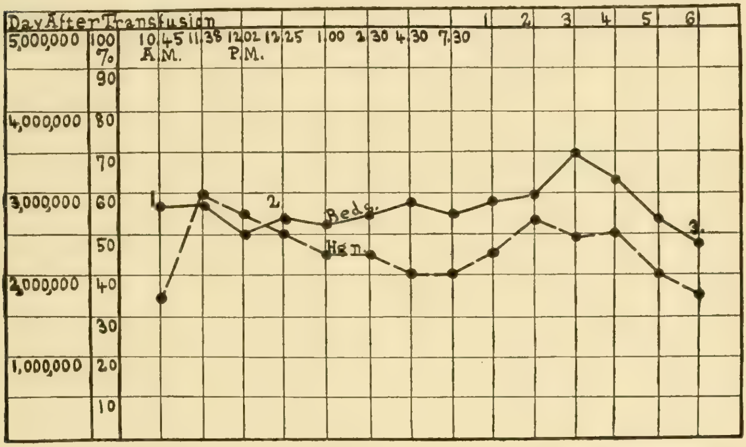


FIG. 62.—CASE NO. IX, 4 (6,492). BLOOD CHART OF RECIPIENT. HEMORRHAGES IN TYPHOID FEVER. 1, 2. Just before, and soon after transfusion. 3. Death. Duration of transfusion, forty-five minutes.

he had three more. From then he improved until the thirty-second day after entering, when he had a large hemorrhage followed by several small ones, and by still more on the following day.

On the thirty-third day it was decided to transfuse. The donor was a strong young man who had had typhoid fever and who was not related to the patient. The anastomosis was made between the radial artery of the donor and a venous branch at the bend of the elbow of the recipient by the suture method. The blood was allowed to pass over for about forty-five minutes. The color of the lips and nails of the recipient began to improve immediately, and he said that he felt much better. He was returned to the ward in good condition. His hemoglobin had risen from 35 to 55 per cent.

The next day his condition was considerably improved, but on

the day after he had a large hemorrhage of about 20 ounces and several small stools containing darker blood. On the following days there were several more losses of blood. On the sixth day after the transfusion he complained of pain in his right ear, which was followed in about an hour by swelling under the lobe and the development of a marked parotitis. He had been growing steadily weaker all this time. On the seventh day after the transfusion (the fortieth after his admission) the other parotid gland was involved, and rapidly progressing failure ended in death.

Comment.—The patient showed marked temporary improvement. Transfusion did not prevent recurring hemorrhages.

The Recipient

Time	Pulse	Blood-Pressure	Red Count	Hemoglobin	Remarks
10.45 A.M.	128	115 mm.	2,840,000	35%	
11.26 A.M.	...	115 mm.	....	....	Began to transfuse.
11.27 A.M.	...	115 mm.	....	....	
11.28 A.M.	...	115 mm.	....	....	
11.29 A.M.	...	115 mm.	....	....	
11.30 A.M.	...	116 mm.	....	....	
11.31 A.M.	...	117 mm.	....	....	
11.32 A.M.	...	118 mm.	....	....	
11.35 A.M.	...	121 mm.	....	....	Color improving.
11.38 A.M.	...	122 mm.	2,872,000	60%	Facial aspect brightening. Nails and cheeks pinker. Respiration slower and deep.
11.43 A.M.	...	122 mm.	....	....	
11.48 A.M.	...	122 mm.	....	....	
11.52 A.M.	112	124 mm.	....	....	
11.58 A.M.	...	125 mm.	....	....	
12.02 P.M.	...	126 mm.	2,528,000	55%	Color still improving.
12.20 P.M.	104	126 mm.	....	....	Patient says he feels better. Transfusion stopped.
12.25 P.M.	...	....	2,696,000	50%	
1.00 P.M.	...	....	2,600,000	45%	
2.30 P.M.	...	....	2,716,000	45%	
4.30 P.M.	...	....	2,888,000	40%	
7.30 P.M.	...	....	2,728,000	45%	
2d day.	...	....	2,880,000	45%	
3d day.	...	....	2,968,000	53%	
4th day.	...	....	3,472,000	48%	
5th day.	...	....	3,184,000	50%	
6th day.	...	....	2,680,000	40%	
7th day.	...	....	2,392,000	35%	Parotitis. Death.

(See Chart, Fig. 62.)

The Donor

Time	Pulse	Blood-Pressure	Red Count	Hemoglobin	Remarks
10.40 A.M.	...	127 mm.	4,816,000	100%	
10.45 A.M.	120	....	....	....	
10.55 A.M.	132	140 mm.	....	....	
11.05 A.M.	144	137 mm.	....	....	
11.10 A.M.	140	135 mm.	....	....	
11.15 A.M.	140	134 mm.	....	....	
11.20 A.M.	132	132 mm.	....	....	
11.26 A.M.	140	130 mm.	....	....	Transfusion started.
11.29 A.M.	140	130 mm.	....	....	
11.32 A.M.	144	132 mm.	....	....	
11.35 A.M.	144	130 mm.	....	....	
11.39 A.M.	144	130 mm.	....	....	
11.42 A.M.	148	130 mm.	....	....	
11.45 A.M.	148	128 mm.	....	....	Lips getting pale. Sweating freely.
11.49 A.M.	148	135 mm.	....	....	
11.52 A.M.	154	125 mm.	....	....	
11.56 A.M.	154	123 mm.	4,064,000	80%	
12.01 P.M.	154	123 mm.	....	....	
12.06 P.M.	148	123 mm.	....	....	
12.13 P.M.	154	121 mm.	4,000,000	75%	
12.20 P.M.	152	90 mm.	....	....	Transfusion stopped.
12.25 P.M.	124	85 mm.	....	....	
12.30 P.M.	120	80 mm.	3,360,000	65%	

(See Chart, Fig. 20, p. 114.)

Case No. IX, 5 (6,539). Abstract. Consultation with Drs. J. N. Gallagher and J. V. Kofron.

Typhoid Fever; Intestinal Hemorrhages of Increasing Severity; Profound Collapse; Transfusion from Immune Donor; Complete Resuscitation; Continuance of Hemorrhages; Death on Third Day after Transfusion.

The patient was an American, a young man of unstated age, whose family history was negative and whose personal history was also negative except for an attack of "dysentery" at some unknown time.

About fifteen days before entering the hospital the patient had had headache, insomnia, profuse perspiration at night, and loss of appetite and strength, and had vomited several times. When he entered the hospital it was found that he had a temperature of 103° F., a pulse ratē of 96 per minute, a coated tongue, a peculiar vasomotor disturbance of the face, a distinctly enlarged spleen and

a slightly enlarged liver, a somewhat distended abdomen, and tenderness over the right iliac fossa. The Widal reaction was positive, and the diagnosis of typhoid fever was made.

The usual typhoid treatment was administered. At the end of the twelfth day slight hemorrhages from the bowels were noticed. They recurred with increased severity and became continuous. The blood loss was so great that, in spite of all endeavor to check it, the patient became unconscious, pulseless, covered with cold perspiration, and sank rapidly. The respirations were shallow. A tracheal tug was noticed. It was thought that transfusion might not only cause the patient to rally from his condition of collapse, but might possibly prevent further hemorrhage.

A brother of the patient who had had typhoid fever served as donor. The anastomosis was made by the suture method in great haste on account of the patient's critical condition. A radial artery of the donor was connected with a venous branch of the patient, and the blood was allowed to flow across for forty-five minutes.

After the blood had flowed for about five minutes, the pulse of the patient could be palpated at the wrist, although very faintly. In about ten minutes a change was noticed in his facial expression. The pulse could then be counted. In fifteen minutes there was a little faint pink color in his ears and lips, the respirations were less frequent, the pulse was of better volume and tension, and his general condition was improved. In twenty minutes the orbits showed marked filling, the lines of the face were beginning to disappear, a little pink color appeared in his cheeks, the blood-pressure was rising and the pulse rate falling. Consciousness was beginning to return. In thirty minutes he became partly rational. His cheeks were still more pink and full and the quality of the pulse was still better. At the end of forty-five minutes the color had spread to all parts of the face, which was then florid. He was not only rational, but even jovial. The respirations were at the rate of 24 per minute. The pulse was fully established in tension and volume. He was then taken back to his room and the usual treatment begun again. His condition was most encouraging. The transformation was remarkable.

At the end of forty-five minutes the donor fainted. The changes which he underwent were just the opposite of those occurring in the recipient—a steadily increasing pallor, free sweating, quickened, shallow respiration, quickened and progressively weaker pulse, etc. In short, if the process had been allowed to proceed long enough, the positions of donor and recipient would have been reversed as far as their general welfare was concerned.

Unfortunately, the hemorrhages from the bowels of the patient continued the next day, and steadily increased until death occurred on the third day after the transfusion.

Comment.—The definite plan of operation in this case was, first, to test the power of similar immune blood to resuscitate a patient in such a state of collapse; and second, to test the value of the transfused blood as a means of preventing further hemorrhage. The first part was successful beyond the greatest expectation, but the influence in arresting the hemorrhage was *nil.* If operative measures had seemed to be advisable, the transfusion had made the patient a good risk.

The statistics of the donor are as follows:

The Donor

Time	Red Cells	Hemoglobin
Just before	5,500,000	100%
Just after	4,250,000	80%

(See Chart, Fig. 21, p. 115.)

Case No. IX, 6 (6,408). Abstract. Consultation with Dr. F. J. Schmoldt.

Exploratory Laparotomy; Diagnosis of Nephrolithiasis; Lumbar Nephrotomy; Removal of Calculi; Uncontrollable Secondary Hemorrhage for Thirteen Days; Acute Cystitis; Suprapubic Drainage of Bladder; Transfusion; Cessation of Hemorrhage; Healing of Lumbar Wound; Nonhealing of Abdominal Wound; Peritonitis; Death Ten Days after Transfusion.

The patient was a German, forty-seven years of age, with a negative family history and a personal history of an attack of typhoid fever five years previously. He denied having had venereal disease.

Five years previously he also had had an attack of severe pain in his left side and loin, which had returned at intervals up to six weeks previously, when he had had a very severe attack. For the last four weeks of this time he was unable to work, but at no time was he confined to his bed. He saw several physicians, some of whom believed that his progressive loss of weight, abdominal pain,

and a certain amount of mucus in his stools indicated the presence of a malignant growth in the bowels. On account of circumstances making it impossible to have an X-ray photograph taken, and on account of the uncertainty of the diagnosis, it was decided to perform an exploratory laparotomy. The urinary analyses did not throw any light on the matter that was considered definitive.

An incision was made to the left of the median line, and the abdominal cavity explored through it with negative results. The left kidney, however, was then palpated and found to be thickened and high up in the body cavity. The abdominal wound was closed and the patient placed ready for the usual lumbar incision. On cutting down to the kidney it was found to be enlarged, congested, and edematous, and stones could be easily palpated. The renal pelvis was opened and a large stone, 2½ by 3¼ cm. was removed, as well as two small stones from the calices. There was brisk bleeding when the incision was carried through the granulation tissue in which the larger stone was lying. This was controlled by sutures and iodoform gauze packing.

The patient did well until five days after the operation, when secondary hemorrhage appeared in the form of a continuous persistent oozing, which lasted thirteen days in spite of all the efforts to check it. At this time the red count was reduced to 1,800,000, the hemoglobin to 20 per cent, and the patient had been delirious for two days. Transfusion was strongly urged, but was opposed until it was obvious that the patient had reached the terminal stage.

At the time of the transfusion the patient was wildly delirious, and it was only with great difficulty that he could be restrained enough to permit the execution of the technical part of the operation. The donor of the blood was a man who was not related to the patient. The anastomosis was made in the usual way from the radial artery of the donor to one of the superficial arm veins of the recipient, the suture method being employed. The blood was allowed to flow across for forty-five minutes.

At the end of ten minutes of transfusion the patient's delirium had gradually lessened. At the end of twenty minutes it had entirely ceased, and his mental state was clear. At the end of the transfusion the hemoglobin had risen to 50 per cent, the blood-pressure from 68 mm. to 102 mm. of mercury, the pulse had fallen from 130 to 110 beats per minute, and the general condition was satisfactory.

After the transfusion the hemorrhage (which was then entirely into or from the bladder as the lumbar wound had entirely healed) gradually ceased and at no time returned. As the patient had been

in such a weakened condition for so long a time, the abdominal wound showed no signs of repair, and, moreover, the continued bleeding into the bladder and accumulation of clots led to a very severe acute cystitis, which necessitated the performing of a suprapubic cystotomy and permanent drainage for a certain length of time. In the violent delirium the dressings were torn away at various times, and the abdominal wound was soaked with infected urine. This unfortunate and unavoidable occurrence led to infection and breaking down of the wound, so that the patient died ten days after the transfusion from an intractable peritonitis.

Comment.—In this case the previously uncontrolled bleeding was completely controlled through the transfusion. The difficulties presented from the renal side of the case were, therefore, surmounted, but death occurred from peritonitis following infection of the abdominal wound due to the struggles of the patient while in delirium. If the transfusion could have been performed earlier the patient's chances of recovery would have been excellent.

The statistics are as follows:

THE RECIPIENT

During the Transfusion

TIME	Pulse	Blood-Pressure	Hemoglobin	Remarks
11.45 A.M.	130	68 mm.	30%	
11.50 A.M.	...	....	....	Began to transfuse.
11.55 A.M.	116	76 mm.	....	
12.00 M.	116	75 mm.	....	
12.05 P.M.	116	76 mm.	....	
12.08 P.M.	...	78 mm.	....	
12.11 P.M.	112	84 mm.	....	
12.12 P.M.	...	85 mm.	....	
12.15 P.M.	112	....	35%	
12.17 P.M.	...	84 mm.	....	
12.20 P.M.	110	....	....	
12.22 P.M.	...	88 mm.	....	
12.39 P.M.	...	88 mm.	....	
12.40 P.M.	112	....	....	
12.45 P.M.	...	92 mm.	40%	
12.50 P.M.	110	102 mm.	....	Stopped transfusing.

NOTE.—The apparent discrepancy between the interval which the flow lasted as shown by these figures, and the stated time of forty-five minutes (see text) is due to allowance being made for short periods of stopping the flow which are not stated in the above. The next day the hemoglobin had risen to 50 per cent.

THE DONOR

During the Transfusion

Time	Pulse	Blood-Pressure	Hemoglobin	Remarks
11.10 A.M.	80	130 mm.	100%	
11.50 A.M.	80	....	....	Began to transfuse.
12.00 M.	80	....	....	
12.05 P.M.	74	....	....	
12.20 P.M.	72	....	....	
12.25 P.M.	72	....	....	
12.28 P.M.	..	97 mm.	80%	
12.50 P.M.	72	....	....	Stopped transfusing.

CASE NO. IX, 7 (6,540). ABSTRACT. CONSULTATION WITH DR. D. S. HANSON.

Repeated Hemorrhages from the Bowels Lasting Several Months; Profound Secondary Anemia; Transfusion; Cessation of Hemorrhages and Marked General Improvement; Slight Bleeding at End of Three Weeks; Rectal Ulcers Sutured; Restoration to Health; No Recurrence of Bleeding in Two Years and Three Months.

The patient was a Bohemian woman, fifty-four years of age, with an excellent family history. She had had the usual diseases of childhood, and smallpox when she was thirty years old. There was nothing in her own or her family history which indicated that hemophiliac or other pathologic hemorrhage had ever occurred.

For several years previously she had had occasional bleeding from the bowels. Five months previously she had had a severe hemorrhage while at stool, and several discharges of blood later in the same day. Before this occurred she had been constipated. From that time on she passed blood with every stool. She would have a desire to go to stool many times a day, and would pass a little blood with each stool. She became greatly reduced, although under treatment from the time of the first hemorrhage up to the time of the transfusion. Four months previously she had had a severe vomiting attack which lasted two weeks. The vomiting persisted at intervals after this time throughout. She had fainted on many occasions, had had marked backache, no abdominal pain or fever, had but little appetite, and lost weight steadily. She consulted several physicians, but treatment of all sorts by mouth, by enemata, or by suppository failed to give relief. Finally, she became bedridden, and transfusion was proposed.

Just before the transfusion the physical examination showed that

the patient was greatly emaciated. Her skin was of a deep lemon-yellow color, and no pink tinge from the circulating blood could be observed in any superficial part of her body. The extremities were edematous. No tumor could be found, and there were no hemorrhoids, fissures, or a fistula. She had no appetite and refused food. A very marked hemic murmur was heard over the heart. The pulse was 112, of low tension and dicrotic, and the temperature was slightly subnormal. The blood examination showed a red count of 1,200,000 cells per cubic millimeter. The hemoglobin was reduced to 12 per cent. Owing to the urgency of the case a more extensive blood examination could not be made.

At the transfusion a son of the patient served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method, and the blood was allowed to flow across for about fifty-eight minutes.

As the flow progressed the changes resulting in the patient's face were most striking. The lemon-yellow color gave way, not to a pinkish tinge at first, as would have been expected, but to a dirty white pallor which later changed to the normal pinkish color. An interesting fact which was noted was that the pallor did not appear all over the face at one time, but came out rather irregularly, leaving " islands " of yellow surrounded by it. As the " islands " gradually faded to the pallor the pink shades replaced the latter, and spread until the entire face was colored. While this was going on the skin was losing its deeply wrinkled appearance and filling out almost as if air had been injected under it. The ears and lips lost their waxlike appearance and became more and more pink. The hands and nails also resumed their normal appearance. Everyone who saw the changes in the face agreed that the most striking thing of all was that the patient was transformed from a wrinkled, corpselike old woman of from sixty-five to seventy years of age to as strong and well looking a woman as one would expect to see who had just passed the half-century mark.

As would be expected with such a transformation of appearance, there was a corresponding physical and mental improvement. The weakness of such extreme degree was replaced at once by the return of considerable strength, although, of course, after such an illness the full strength was not regained until several weeks later. The pulse was improved in rate and quality, the nausea and vomiting ceased, the subnormal temperature was replaced by normal temperature, and the first meal offered to the patient was eaten with relish, in striking contrast to her previous refusal of food.

An entirely unexpected outcome (this was one of the earliest cases in which transfusion was employed) was the immediate and complete arrest of the hemorrhages from the rectum. The object which it was hoped would be obtained by the transfusion was that the patient would be revived enough to permit her being anesthetized, and a thorough rectal examination made which the previous circumstances did not permit. For the time being this was not neces-

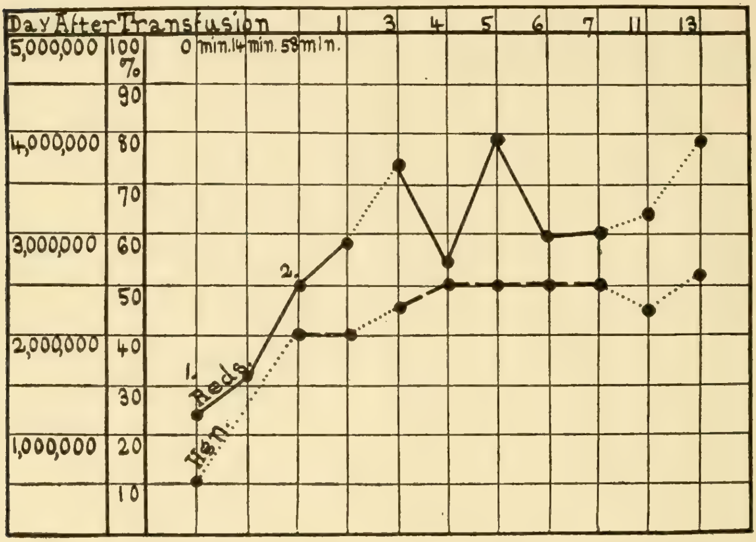


FIG. 63.—CASE NO. IX, 7 (6,540). BLOOD CHART OF RECIPIENT. RECTAL HEMORRHAGES. 1, 2. Just before, and just after transfusion. Duration of transfusion, fifty-eight minutes.

sary on account of the control of the hemorrhages. Immediately after the transfusion the red cells had risen from 1,200,000 to 2,450,000, and the hemoglobin from 12 to 40 per cent.

Three weeks after the transfusion a little blood was noticed in the stool. She was then examined, and small ulcers of the rectum and a varicose condition were found. The ulcers were sewed over, and no more blood was passed.

The history of the patient subsequent to the transfusion was one of rapid and uninterrupted progress. When she returned to her home she took up her household duties again. Two years and three months after the transfusion she had had no return of the hemor-

rhage. Her red count at this time was 4,600,000 cells per cubic millimeter and her hemoglobin 85 per cent.

Comment.—With a patient in the terminal stage of secondary anemia from hemorrhage from the rectum, transfusion was proposed after all other means of treatment had failed. It was merely hoped that the transfusion would so improve the condition that it would be safe to give an anesthetic so that the source of bleeding might be searched for and possibly secured. The arrest of the hemorrhage by the transfusion alone was entirely unexpected.

The statistics are as follows:

The Recipient

Time	Pulse	Red Count	Hemoglobin	Remarks
0 minute.	100	1,200,000	12%	Transfusion begun.
2 minutes.	104	....	....	
4–8 minutes.	100	....	....	
10–18 minutes.	98	1,560,000	....	
20 minutes.	100	....	....	
22–26 minutes.	98	....	....	
28 minutes.	96	....	....	
30 minutes.	96	....	....	
32–36 minutes.	92	....	....	
38 minutes.	88	....	....	
40 minutes.	86	....	....	
42 minutes.	88	....	....	
44 minutes.	86	....	....	
46 minutes.	86	....	....	
48–54 minutes.	88	....	....	
56 minutes.	90	....	....	
58 minutes.	90	....	....	Transfusion ended.
60 minutes.	...	2,450,000	40%	
1st day.	...	2,900,000	40%	
3d day.	...	3,680,000	45%	
4th day.	...	2,700,000	50%	
5th day.	...	3,800,000	50%	
6th day.	...	2,972,000	50%	
7th day.	...	3,000,000	50%	
11th day.	...	3,152,000	45%	
13th day.	...	3,900,000	55%	
13 months.	...	4,600,000	85%	

(See Chart, Fig. 63.)

NOTE.—The blood-pressure was not measured by means of the Riva-Rocci apparatus, but a steady rise in the pressure accompanied the fall in the pulse rate during the transfusion.

Case No. IX, 8 (6,854 and 6,957). Abstract. Consultation with Dr. Woessner.

Hemorrhage from the Bowels of Unknown Origin; Failure of Treatment for More than One Year; First Transfusion; Slight Improvement Only; Second Transfusion at End of Three Months; Immediate Change from Diarrhea to Constipated Condition with Beginning Diminution of Amount of Blood in Stools; Total Disappearance of Blood by End of Four Weeks; No Return of Blood by End of Nine Weeks.

The patient was an American, forty-nine years of age, with a negative family history as regards tuberculosis, neoplasm, and hemophilia. He did not remember having had any of the ordinary diseases of childhood. He used alcohol in moderation and denied having had gonorrhea or syphilis.

His complaint was that he had blood in his stools. Three years previously he had begun to have hemorrhoids. One year previously they were removed by operation, and since that time he had never been constipated as he formerly was, but had had diarrhea, with sometimes as many as 15 bloody stools a day. Occasionally the stools contained no blood. At times he passed white pus-like material mingled with the stool. Since the beginning of his trouble he had had general abdominal uneasiness, but never any pain. He usually passed much flatus. He had had no night sweats. He weighed more than when first taken sick.

The physical examination showed the patient to be a fairly well nourished man with mucous membranes of good color, and with no general glandular enlargement. His heart and lungs were apparently normal. The abdomen presented normal fullness and resistance to pressure. No masses could be palpated. Over the left iliac fossa there was tenderness, and what was thought to be the sigmoid flexure was palpated. Palpation of the rectum revealed nothing abnormal, and a further examination showed that the blood must have come from some place too high to be seen by means of the proctoscope. The epididymis and shins were normal. A careful search for tubercle bacilli and amebæ was negative.

On the ground of the results obtained in similar cases, and from the fact that in a year no treatment had been found which controlled the bleeding, it was decided to transfuse.

At the first transfusion a nephew of the patient served as donor. He was seventeen years old and weighed 180 pounds. One of his radial arteries was anastomosed to a median basilic vein of the

patient by the cannula method. Before the blood was allowed to flow across the latter was bled 300 c.c. The flow was allowed to continue for twenty minutes.

As a result of the transfusion there was no marked facial change in either donor or recipient. The red count of the latter before bleeding was 4,640,000, the hemoglobin 90 per cent, and the white count 7,720. After the transfusion the red count had risen to 5,056,000, the hemoglobin was unaffected, and the white count rose to 9,200. As the blood taken away was merely replaced with new blood, there was no particular change in the symptoms of the recipient during and immediately after the transfusion.

For a short time there was slight improvement in the quality of the stools, but there was no marked improvement. It was thought that this might be due to less blood having been transfused than on other similar occasions. After the patient was discharged from the hospital the condition persisted with possibly some improvement. Three months after the first transfusion it was decided to try the effect of another.

At the second transfusion the donor was not related to the patient. One of his radial arteries was anastomosed to the other median basilic vein of the patient as before. This time the patient was not previously bled. The blood was allowed to flow across for about twenty-five minutes.

Immediately after the transfusion the red count of the patient had risen from 3,328,000 to 4,416,000, the hemoglobin from 80 to 85 per cent, and the white count was 10,400 (no count was made before the transfusion). There was marked gastric disturbance (nausea and retching) which persisted for a week or ten days. The diarrhea was immediately replaced by constipation, and the amount of blood in the stools began immediately to decrease.

Four weeks after the second transfusion there was no blood in the stools. Nine weeks after there had been no recurrence, and the patient considered that he was entirely well.

Comment.—This case is of particular interest on account of the patient receiving blood from two different donors in a period of a little less than three months without any sign of hemolysis developing at any time. As in Case No. IX, 1 (6,411) no trouble was experienced from this source. The

necessity for the second transfusion apparently indicates that the question of dosage may be important. It is possible, however, that the blood of the second donor contained elements which were not present in that of the first donor, and that the arrest of the hemorrhages was due to this rather than to the increased amount of blood transfused.

The statistics are as follows:

THE RECIPIENT

First Transfusion

TIME	Red Count	Hemo-globin	White Count	Platelets	Coag. Time	Sp. Gr.
Day before......	4,640,000	90%	7,720	......	.....	....
Just before......	....	....	....	520,000	3′ 50″	1,060
Just after.......	5,056,000	90%	9,200	......	.....	....
2d day..........	4,920,000	90%	8,400	460,000	4′ 00″	1,060

During the Transfusion

TIME	Blood-Pressure	Pulse	Respiration
Just before..................	145 mm.	84	16
End of five minutes..........	140 mm.	152	40
End of fifteen minutes.......	156 mm.	84	20
End of twenty minutes.......	165 mm.	72	16

NOTE.—No statistics were obtained at the second transfusion further than those already stated in the text.

THE DONOR

First Transfusion

TIME	Red Count	Hemoglobin	White Count
Just before......................	5,312,000	100%	7,440
End of five minutes..............	5,350,000	100%	8,000
End of fifteen minutes...........	5,280,000	100%	10,000
Sixteen minutes after transfusion...	5,360,000	100%	10,000
Forty-eight hours after..........	5,328,000	100%	8,960

(See Chart, Fig. 22, p. 117.)

The Donor—(*Continued*)

During the Transfusion

Time	Blood-Pressure	Pulse	Respiration
Just before	135 mm.	84	16
End of ten minutes	125 mm.	80	16
End of twenty minutes	150 mm.	80	16
End of thirty minutes	120 mm.	84	16

Case No. IX, 9 (6,663). Abstract.

Hemorrhage from Bowels of Eighteen Months' Duration of Tuberculous Origin; Failure of Treatment to Control Hemorrhage; Transfusion; Gradual Cessation of Hemorrhage; Occasional Trace of Blood and Some Colitis at the End of Sixteen Months; General and Local Condition Very Much Improved.

The patient was an American, thirty years of age, whose complaint was hemorrhage from the bowels. His family history was unimportant except that his mother and several aunts died of tuberculosis. There was no history of hemophilia. His personal history gave no evidence of previous tuberculosis. Six years previously he had had hematuria lasting one day, burning on micturating, and frequency of micturition. He had worked as a foreman for many years without loss of time on account of illness.

Eighteen months previously he had first noticed bright blood on the surface of his stools, and from that time until he entered the hospital it was almost constantly present. He had no pain, gastric disturbance, or hemorrhoids. The amount of blood steadily increased until it was estimated that he was losing 50 c.c. daily. When he entered the hospital quantities of clots were noticed. The hemorrhage was increased by physical exertion. He soon had night sweats and some nocturnal fever. No pus was noticed in his stools. For the last three months he had passed from 4 to 8 stools daily. For two weeks he had had severe occipital headaches and considerable palpitation of the heart.

In the hospital the physical examination was negative as to tuberculosis, tumor, and syphilis. There was slight tenderness in the right iliac fossa. A proctoscopic examination showed the mucous membrane of the entire rectum and of the sigmoid flexure to be edematous, highly congested, and with considerable blood oozing

from its surface. Many examinations of the stools for parasites were negative. On one occasion Dr. L. W. Ladd found tubercle bacilli, but they were never found again, even after repeated examinations. The red count was 4,952,000, the hemoglobin 90 per cent, and the white count 10,400.

The patient was put on liquid diet and kept in bed. The lower bowel was irrigated every day with a solution of argyrol. Each evening there was a rise in temperature. As a general rule the stools were small, liquid in character, and of dark-red color with numerous bright red streaks. There were a good many dark clots, some of them quite large. The patient lost strength steadily, but his blood seemed to be regenerated as fast as it was lost.

In order to study the changes occurring in metabolism after transfusion the patient was brought into as near a state of nitrogenous equilibrium as possible by placing him on a carefully regulated and weighed diet, and by repeated examinations of the twenty-four-hour amounts of urine which he passed. The only proteid substances which he received were those contained in milk, eggs, and beef tea.

The donor was a strong healthy man whose blood was normal, and whose general health was excellent. He was not related to the patient. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method. Before the flow was allowed to begin the patient was bled for twenty minutes in order to avoid overloading his circulation. The blood was allowed to flow across for fifty-four minutes.

In spite of having received the customary ¼ grain of morphin the patient was restless and nervous during the transfusion. His improvement was marked. His lemon-yellow skin became of a normal pinkish hue, his sunken orbits filled out, and his wrinkles nearly all disappeared. At first mentally apathetic, he soon took an interest in his surroundings, and finally became rather buoyant. Two hours after the transfusion began he was sitting propped up in bed eating heartily. The donor showed more marked effects than usual, but soon recovered from them.

The day following the transfusion the temperature of the recipient rose to 101.4° F., and a slight fever continued for several days. The stools immediately had less blood and became more formed in character. On the tenth day no blood was present. At the end of two weeks the patient was discharged, feeling very much stronger,

having better appetite, and having lost his previous despondency. At this time the stools were all formed, and only occasionally was a slight amount of blood noted. Proctoscopic examination showed a striking improvement in the rectal mucosa. The edematous blood-tinged appearance had almost entirely disappeared, and there appeared to be a fairly healthy normal mucosa. There was no blood present except that caused by the introduction of the instrument. The blood examination showed a red count of 5,312,000, as compared with 4,952,000 on admission, and 4,880,000 just previous to being bled before the transfusion.

After the patient left the hospital he had several mild relapses, but the major part of his improvement has been maintained. He returned to work after several months. At the present time, sixteen months after the transfusion, he has only an occasional trace of blood and a mild colitis. His temperature remains normal, he has no night-sweats, his appetite is normal, and he apparently enjoys normal health. No other treatment has been followed since the transfusion.

In regard to the detailed studies of the patient, the following may be said: Before the transfusion the differential blood count was normal. By the end of the preliminary bleeding there was a marked decrease in the number of polymorphonuclear neutrophiles with an increase in the large lymphocytes. By the end of the transfusion the polymorphonuclear leucocytes had risen again, and to a point higher than the original number. This time the large lymphocytes were found to have fallen markedly.

Three days after the transfusion the polymorphonuclear neutrophiles had fallen from the preliminary figure of 74 per cent to 69.1 per cent, showing that the rise immediately after the transfusion was not maintained. The large and small lymphocytes were about normal in percentage. The eosinophiles were found to have increased from normal up to 10.4 per cent. Dr. Moorehouse found that the smears showed a more marked destruction of the polymorphonuclear leucocytes than normally occurs.

Dr. H. D. Haskins made the metabolism study. The entire study of this patient was controlled by Dr. J. J. MacLeod. Careful quantitative analyses of the twenty-four-hour quantities of urine were made during four days before and five days after the transfusion. The nitrogen was estimated by Kjeldahl's method, and ammonia by Folin's method. Examination of the table shows that the patient was excreting about 10.3 gms. of nitrogen before the operation and 0.16 gms. of ammonia, and was voiding between 700

and 800 c.c. of urine with a specific gravity ranging from 1.023 to 1.025. After the transfusion a marked change was found, the nitrogen having risen from 10.3 to 16.5 gms., and the ammonia from 0.16 to 0.47 gms. The change in the ammonia percentage was compensatory. The amount of urine also increased from 800 to 1,095 c.c. in twenty-four hours. Oddly enough the specific gravity rose directly with the amount of urine.

Later there was a gradual drop in the amount of nitrogen with the ammonia falling in definite ratio, so that on the fifth day after the transfusion it was slightly below that just previous to the transfusion, and by the end of the experiment had returned practically to the original amount.

Comment.—While there were several mild relapses after the transfusion, the general results must be considered as excellent. A permanent cure may or may not have been established, but at least the general and local improvement is marked.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count	Coag. Time	Sp. Gr.	Remarks
Dec. 16th.	4,952,000	90%	10,400	.....	.....	
Jan. 8th.	5,312,000	....	8,000	.....	1.059	
Jan. 9th.	5,216,000	....	7,860	.....	1.059	
Jan. 10th.	4,936,000	....	5,840	.....	1.059	
Jan. 11th.	4,896,000	95%	7,740	4′ 0″	1.059	
Jan. 12th.	4,800,000	95%	6,440	4′ 0″	1.059	
Jan. 13th.	4,880,000	95%	6,040	4′ 0″	1.059	
Jan. 14th.	4,588,000	89%	12,340	4′ 0″	.....	End of bleeding.
Jan. 14th.	4,668,000	....	8,440	.....	.....	End of transfusion.
Jan. 14th.	4,376,000	....	10,040	.....	1.056	Eight hours after transfusion.
1st day.	4,672,000	89%	9,680	5′ 0″	1.057	
2d day.	4,680,000	....	8,740	.....	1.057	
3d day.	4,920,000	....	7,440	.....	1.059	
4th day.	4,688,000	84%	6,800	4′ 30″	1.059	
5th day.	4,440,000	....	5,600	.....	1.059	
7th day.	4,768,000	84%	7,200	5′ 30″	1.058	
11th day.	5,006,000	84%	14,000	5′ 30″	1.059	
12th day.	4,896,000	....	14,440	.....	.....	

(See Chart, Fig. 64.)

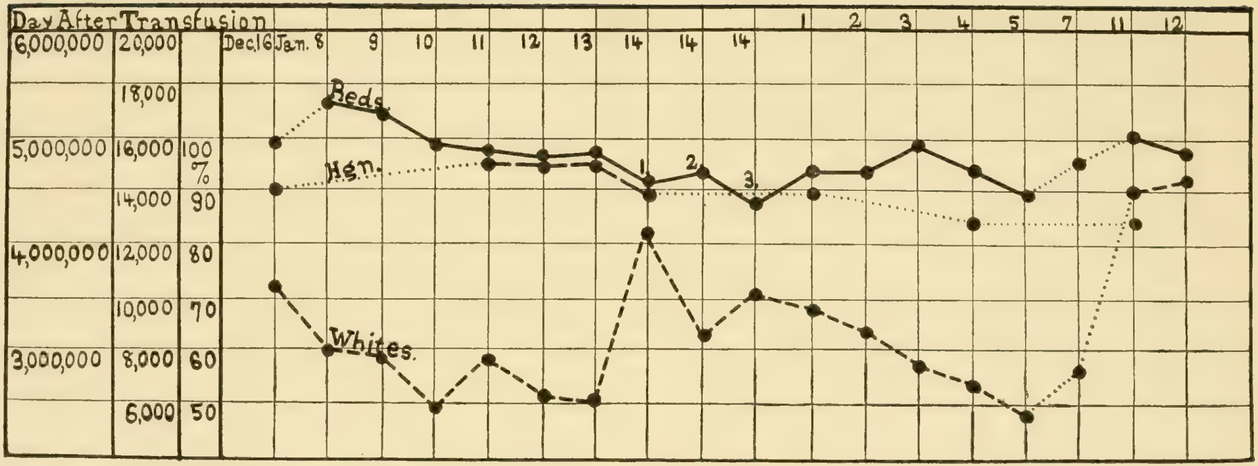


FIG. 64.—CASE NO. IX, 9 (6,663). BLOOD CHART OF RECIPIENT. HEMORRHAGE FROM BOWELS OF TUBERCULOUS ORIGIN. 1. Just after preliminary bleeding (note characteristic fall in red cells and hemoglobin and rise in white cells) and just before transfusion. 2, 3. Just after and eight hours after transfusion. Duration of transfusion, fifty-four minutes.

The Quantitative Analyses of the Urine

Time	Nitrogen	Ammonia [1]	Ammonia in Per Cent	Total 24-Hour Amount	Specific Gravity
Jan. 10th.	10.17 gm.	0.42	4.1%	795 c.c.	1.025
Jan. 11th.	8.71 gm.	0.50	5.7%	710 c.c.	1.027
Jan. 12th.	10.79 gm.	0.36	3.4%	845 c.c.	1.026
Jan. 14th.[2]	10.30 gm.	0.16	1.6%	805 c.c.	1.023
Jan. 15th.	16.52 gm.	0.47	2.8%	1,095 c.c.	1.028
Jan. 16th.	16.12 gm.	0.21	1.9%	725 c.c.	1.030
Jan. 17th.	12.86 gm.	0.16	1.2%	650 c.c.	1.027
Jan. 18th.	8.37 gm.	0.15	1.8%	530 c.c.	1.030
Jan. 19th.	9.13 gm.	0.23	2.5%	725 c.c.	1.027

[1] The ammonia is expressed in terms of nitrogen. [2] The day of the transfusion.

The Donor

Time	Red Count	Hemoglobin	White Count
Day before	5,136,000	100%	8,840
After fifteen minutes	4,956,000	.....	14,420
After thirty minutes	4,996,000	.....	16,140
After fifty-four minutes	4,828,000	80%	35,460
1st day	4,600,000	84%	11,100
2d day	5,216,000	92%	10,240
3d day	5,180,000	100%	7,600
4th day	5,180,000	.....	7,200
6th day	5,278,000	.....	5,800

(See Chart, Fig. 23, p. 118.)

Case No. IX, 10 (6,633). Abstract.

Hemorrhage from the Bowels of Undiscovered Etiology; Continuance for Three Years; Failure of Treatment; Transfusion; Cessation of Hemorrhage; Recovery; No Recurrence in Twenty-five Months.

The patient was an American, twenty-four years of age, with a negative family history, especially as regards hemophilia or tuberculosis. He denied venereal disease. He had had the usual diseases of childhood.

Three years previously he had first noticed that his stools were streaked with blood. He had at the same time a general feeling of abdominal uneasiness and a certain amount of pain. This continued at intervals when his health was good. During the year before the transfusion all the stools were bloody, so that from 5 to 20 c.c. of blood were lost each day in from five to a dozen stools.

They were accompanied with tenesmus, and were composed of scybalæ, mucus, and bright red blood. They were never ribbon-shaped. Sometimes there was diarrhea, and this was present just before the transfusion. The patient's appetite was poor, he had lost approximately 15 pounds in weight, his strength was reduced, and he was unable to work. The blood was little, if at all, altered. The red count was 5,600,000, the hemoglobin 95 per cent, and the white count 13,600. The coagulation time was four minutes. All the different forms of treatment which were tried by several physicians at various times in the three years had failed to control the hemorrhage.

The physical examination showed the abdomen to be slightly scaphoid, and somewhat tender all over on deep pressure. No masses could be palpated even under anesthesia. Neither the spleen nor the liver could be palpated. The rectal examination showed a slightly enlarged prostate, which was firm, rather tender, not nodular, and with the median notch well defined. No masses could be palpated elsewhere. The mucosa of the rectum and the lower sigmoid flexure was intensely congested, and bled from the slightest touch. No ulcers could be seen. Many examinations of the stools failed to reveal tubercle bacilli or amebæ. Transfusion was advised wholly on the ground that the hemorrhage might be due to a chemical alteration of the blood itself.

The donor was a healthy male who was not related to the patient. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method. The blood was allowed to flow across for thirty minutes. Before the transfusion the patient was bled freely.

During the transfusion the patient had no unusual sensation except a feeling of warmth gradually spreading through his previously cold back and extremities. His face gradually filled, the superficial vessels became dilated, the cheeks and mucous membranes became pink, and the volar aspects of the fingers became fuller and took on better color. He had a feeling of buoyancy and of added strength.

Immediately after the operation the previous diarrhea was replaced by constipation, for which it was necessary to give large doses of castor oil. From the very first there was diminution in the amount of blood. When discharged from the hospital three weeks later there was only an occasional streak of blood and mucus.

The patient returned to his former occupation and kept a careful record of every stool he passed during the following twenty-five months. There were but two or three times that there was the slightest amount of blood or mucus passed. His health was always good,

and he said that the warmth which he first noticed after the transfusion had persisted. He had received no other treatment since the transfusion.

Comment.—While the complete cessation of hemorrhage in this case was not immediate, it was evident that the treatment was eventually none the less efficient. The preliminary blood-letting was necessary to avoid overfilling the circulatory system with the transfused blood.

CASE NO. IX, 11 (6,538). ABSTRACT.

Hemorrhage from the Rectum; Operation for Hemorrhoids; Severe Hemorrhage Ten Days after Operation; Continued Intractable Hemorrhage for Eleven Days; Transfusion; Cessation of Hemorrhage Without Return in Eighteen Months; Recovery.

The patient was a German, twenty-seven years of age, with a negative family history. He had not had the usual diseases of childhood.

When he was a child he had had a fall which was followed by severe hemorrhage from the rectum. Since that time he had always had more or less hemorrhage, which was worse when straining at stool or when suffering from a cold. At stool he had also had some prolapse of the rectum, and when this occurred the hemorrhage was made still worse. Twenty-one days previously he had been operated on for hemorrhoids and apparently made a good recovery, leaving the hospital at the end of ten days. On the next day he had had a severe hemorrhage, and returned to the hospital. On the thirteenth day after the operation Dr. Lower sutured the bleeding points, but hemorrhage from the tissues appeared and persisted up to the day of the transfusion.

The donor was a brother of the patient. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the suture method. The blood was allowed to pass over for fifty-five minutes. At the end of the transfusion the hemoglobin had increased from 25 per cent to 65 per cent, and the red count from 1,316,000 to 1,928,000. The immediate stimulating effect of the new blood was very marked. The bleeding ceased in a short time.

The subsequent history showed that the patient rapidly regained his usual health and strength, and soon attained a greater weight than he had ever had before. He returned to his work, and has been in normal health ever since. Twenty-five months after the operation

he reported that he had had no recurrence of the hemorrhage, but that if he had a constipated stool there was an occasional streak of blood.

Comment.—The marked tendency of this patient to hemorrhage suggested in certain aspects that occurring in hemophilia. The behavior of the bleeding, which was largely of so-called tissue origin, in beginning thirteen days after the operation and in proving almost intractable was like the bleeding of hemophilia.

The statistics are as follows:

The Recipient

Time	Pulse	Blood-Pressure	Hemoglobin	Red Count	White Count	Remarks
9.00 A.M.	1 16	118 mm.	25%	1,316,000	......	
9.10 A.M.	...	125 mm.	....	....	......	
9.20 A.M.	...	....	....	....	......	Began to transfuse.
9.25 A.M.	...	132 mm.	....	....	......	
9.30 A.M.	112	....	....	....	......	
9.34 A.M.	...	136 mm.	....	....	......	
9.45 A.M.	104	135 mm.	65%	1,706,000	......	
9.50 A.M.	100	134 mm.	....	....	......	
10.00 A.M.	104	144 mm.	65%	....	......	
10.05 A.M.	...	148 mm.	....	....	......	
10.15 A.M.	140	155 mm.	65%	1,928,000	......	Stopped transfusing.
11.20 A.M.	130	115 mm.	50%	2,208,000	......	
12.20 P.M.	...	....	50%	2,240,000	24,400	
2.15 P.M.	106	105 mm.	55%	2,108,000	22,000	
4.30 P.M.	98	112 mm.	55%	2,316,000	18,000	
6.30 P.M.	100	115 mm.	60%	2,820,000	17,500	
8.30 P.M.	99	115 mm.	60%	2,980,000	18,000	
1st day.	...	....	....	....	......	
10.00 A.M.	94	113 mm.	60%	3,040,000	20,200	
2.00 P.M.	96	115 mm.	60%	2,950,000	21,300	
6.00 P.M.	94	115 mm.	60%	2,870,000	18,000	
2d day.						
3.00 P.M.	100	115 mm.	60%	2,400,000	14,660	
7.00 P.M.	98	120 mm.	60%	2,504,000	14,200	
3d day.						
2.00 P.M.	95	118 mm.	60%	2,840,000	15,000	
8.00 P.M.	94	120 mm.	60%	3,100,000	13,000	
4th day.	96	118 mm.	60%	2,860,000	14,000	
5th day.	93	118 mm.	60%	2,780,000	13,700	
6th day.	94	120 mm.	60%	2,840,000	12,600	
7th day.	90	115 mm.	65%	3,040,000	10,000	

(See Chart, Fig. 65.)

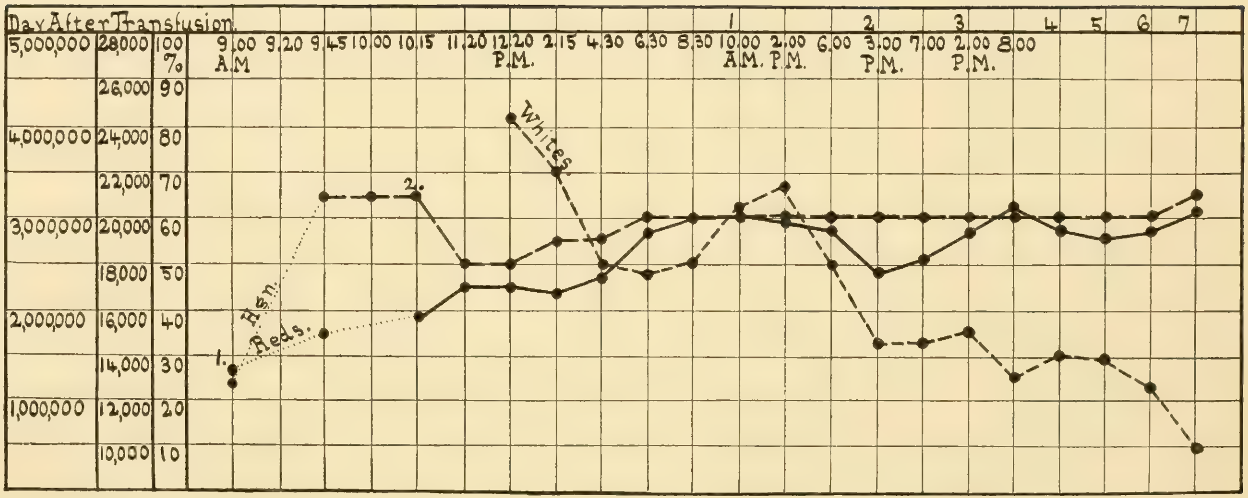


FIG. 65.—CASE NO. IX, II (6,538). BLOOD CHART OF RECIPIENT. HEMORRHAGES FROM RECTUM. 1, 2. Just before, and just after transfusion. Duration of transfusion, fifty-five minutes.

The Donor

Time	Pulse	Blood-Pressure	Hemo-globin	Red Count	White Count	Remarks
8.50 A.M.	68	148 mm.	....	....	......	
9.15 A.M.	..	144 mm.	100%	4,776,000	......	
9.20 A.M.	..	....	.....	....	......	Began to transfuse.
9.31 A.M.	62	....	90%	....	......	
9.37 A.M.	62	140 mm.	.....	....	......	
9.55 A.M.	60	135 mm.	80%	4,752,000	......	
10.08 A.M.	..	140 mm.	.....	....	......	
10.15 A.M.	..	....	.....	....	......	Stopped transfusing.
10.40 A.M.	..	....	75%	....	......	
11.20 A.M.	50	135 mm.	.....	....	......	
11.40 A.M.	..	....	75%	4,032,000	10,800	
3.00 P.M.	60	126 mm.	100%	4,160,000	8,800	
4.30 P.M.	52	135 mm.	100%	4,318,000	9,000	
6.30 P.M.	60	145 mm.	100%	4,640,000	9,200	
1st day.						
11.00 A.M.	84	140 mm.	100%	5,020,000	9,400	
6.15 P.M.	72	140 mm.	100%	4,600,000	9,600	
2d day.	62	138 mm.	100%	5,210,000	8,800	
3d day.	60	135 mm.	100%	5,110,000	10,000	
4th day.	72	138 mm.	100%	5,010,000	8,600	

(See Chart, Fig. 24, p. 119.)

Case No. IX, 12 (6,605). Abstract.

Essential Renal Hematuria; Great Weakness of Patient; Transfusion; Revival of Patient; Nephrectomy; Complete Recovery; Patient Well Twenty-two Months after Transfusion and Operation.

The patient was an American, sixty-nine years of age, with a negative family history as far as the condition treated was concerned. He had had the usual diseases of childhood, dyspepsia, and intestinal trouble for forty-three years since leaving the army, typhoid fever ten years previously, and shortness of breath and palpitation of the heart on exertion for a short time.

Five years previously he had noticed blood constantly in his urine for ten days. No cause of this was apparent. Up to three years previously blood was present off and on regardless of whether he exercised or not. He then passed three "stones," and no more blood appeared for twenty-one months. When he passed the "stones" he had renal colic, great pain, and prostration. Two

months previously he had had frequency of micturition. When examined it was found that he had lost about 15 pounds in weight. He looked thin and emaciated, and was obviously a poor surgical risk. He had a mitral lesion. He had passed blood clots within a short time. From the history and ureteral catheterization by Dr. Lower the diagnosis of essential renal hematuria was made after eliminating other possible affections. Transfusion was decided on in order, if possible, to make a surgical risk which it would be safe to assume.

A son of the patient acted as donor, and one of his radial arteries was anastomosed to a venous branch near the patient's elbow by

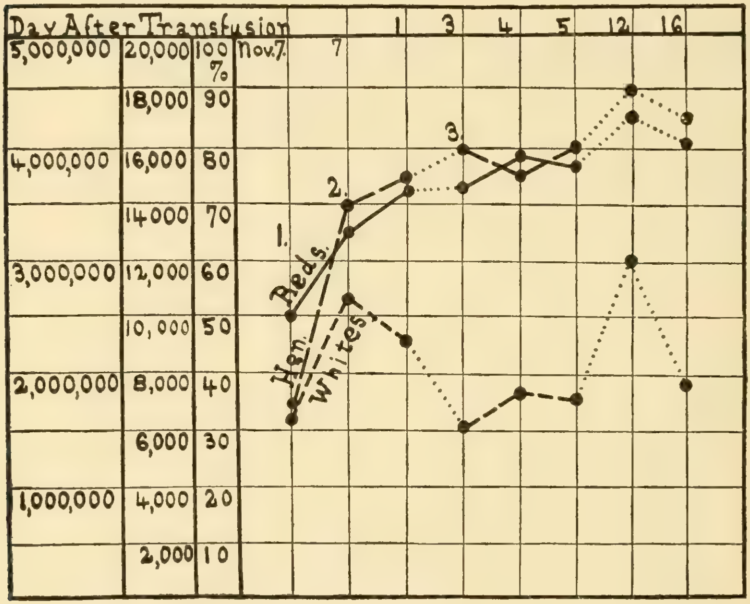


FIG. 66.—CASE NO. IX, 12 (6,605). BLOOD CHART OF RECIPIENT. ESSENTIAL RENAL HEMATURIA. 1, 2. Just before, and just after transfusion. 3. Nephrectomy. Duration of transfusion, forty minutes.

the suture method. The blood was allowed to pass across for forty minutes.

Just before the transfusion the patient's red count was 2,500,000, his hemoglobin 35 per cent, and his white count 6,400. Just after the transfusion the red count had risen to 3,280,000, the hemoglobin

to 70 per cent, and the white count to 10,600. A marked change in the color of his lips, ears, and cheeks was noticed, and he felt very much stronger. His previously shrunken, wrinkled face was filled out. There was a corresponding improvement in his mental condition.

Two days after the transfusion the kidney was removed, the bleeding having continued in the meanwhile. The patient stood the operation without the slightest difficulty. His recovery was complete and uninterrupted, and he was discharged as cured on the sixteenth day after entering the hospital. Gross and microscopic examinations of the extirpated kidney confirmed the diagnosis—at least no other explanation for the hemorrhage could be found.

Comment.—While the transfusion did not diminish the hemorrhage, it converted the patient from a poor to a good surgical risk. The patient has remained well twenty-two months.

The statistics are as follows:

The Recipient

Time	Red Count	Hemoglobin	White Count	Coag. Time	Specific Gravity
Before.[1]	2,500,000	35%	6,400	2′ 15″	1.033
After.[2]	3,280,000	70%	10,600	.....	1.041
1st day.	3,632,000	75%	9,200	2′ 0″	1.042
3d day.	3,656,000	80%	6,000	6′ 22″	1.045
4th day.	3,920,000	75%	7,400	2′ 55″	1.043
5th day.	3,840,000	80%	7,000	3′ 0″	1.040
12th day.	4,272,000	90%	12,000	.....	.....
16th day.	4,056,000	85%	7,600	2′ 0″	1.040

[1] Before the transfusion. [2] After the transfusion.

(See Chart, Fig. 66).

The Pulse and Blood-Pressure During the Transfusion

Time	Pulse	Blood-Pressure	Remarks
5.15 P.M.	...	112 mm.	
5.43 P.M.	...	....	Began to transfuse.
5.45 P.M.	180	123 mm.	
6.00 P.M.	76	135 mm.	
6.20 P.M.	72	135 mm.	
6.30 P.M.	...	....	Stopped transfusing.
7.00 P.M.	...	135 mm.	

THE DONOR

The Pulse and Blood-Pressure During the Transfusion

TIME	Pulse	Blood-Pressure	Remarks
5.05 P.M.	...	110 mm.	
5.10 P.M.	84	90 mm.	
5.15 P.M.	...	90 mm.	
5.20 P.M.	96	120 mm.	
5.25 P.M.	...	125 mm.	
5.30 P.M.	...	120 mm.	
5.35 P.M.	96	....	
5.40 P.M.	...	122 mm.	
5.43 P.M.	...	....	Began to transfuse.
5.45 P.M.	88	108 mm.	
5.55 P.M.	84	115 mm.	
6.00 P.M.	...	115 mm.	
6.10 P.M.	76	100 mm.	
6.15 P.M.	76	110 mm.	
6.30 P.M.	...	....	Stopped transfusing.
6.32 P.M.	...	95 mm.	The donor fainted.
6.40 P.M.	72	95 mm.	

CASE NO. IX, 13 (6,537). ABSTRACT. CONSULTATION WITH DRS. A. AND S. PESKIND, CLEVELAND, OHIO.

Chronic Icteric Condition; Nasal, Uterine, Rectal, and Subcutaneous Hemorrhages; Collapse; Transfusion; Marked General Improvement with Cessation of all Hemorrhages; Exploratory Incision; Diagnosis of Inoperable Carcinoma of Gall Bladder and Adjacent Parts; Death from Carcinoma Seventy-four Days after Transfusion Without Return of Hemorrhages.

The patient was a married woman, forty-two years of age, whose maternal grandmother died of a gastric disorder which may possibly have been carcinoma. Otherwise her family history was negative. Except for the usual diseases of childhood and a miscarriage four years previously her personal history was also negative.

For a year previously her health had become gradually impaired. About three months previously she was taken with an attack of vomiting, and at this time she became jaundiced, had gray stools and highly colored urine, but had neither pain nor fever. Her attending physician considered that there was complete obstruction of the flow of bile. A week previously she had had severe epigastric pain and two small gallstones were passed. The menstrual period fell

due shortly before this, and as the flow lasted for twelve days she was curetted by Dr. Peskind. At about the same time it was noticed that she was having small amounts of blood in each stool. A mass was palpated in the region of the gall bladder.

When first seen by the author her pulse and temperature were elevated and her face was blanched. As before, a hard tender mass could be palpated in the region of the gall bladder. There were a number of petechial hemorrhages, as well as diffuse discolorations of the skin. The rectal bleeding continued. In the evening of the same day she passed into a state of collapse, so that she could not be sent to the hospital. She then had nasal and uterine hemorrhage, as well as from the other parts of the body. Transfusion was performed at home with the hope that the addition of fresh blood to her own blood would stop the hemorrhage.

A brother of the patient served as donor. One of his radial arteries was anastomosed to a venous branch near the elbow of the patient by the suture method. The fact that the artery was unusually large caused some doubt as to the possibility of making a tight connection, but this was accomplished without any trouble. A continuous flow of blood was maintained for forty minutes, when it was discontinued on account of the donor showing signs of fainting.

With the flow of blood the pulse rate of the recipient fell from 110 to 80 per minute, the blood-pressure steadily rose, the face gradually filled out, and the lips and ears became pink. On account of the deep jaundice, the effect on the color of the skin could not be clearly appreciated. Her condition rapidly improved, and at the end of the transfusion she had passed out of her state of collapse and felt stronger and refreshed. During the transfusion the bleeding from the nose stopped. Immediately following it the bleeding from the uterus also stopped. No further subcutaneous bleeding appeared.

The patient passed a comfortable night. The next morning she was in such good condition it was decided to make an exploratory incision under cocain anesthesia in order to discover, if possible, the cause of the obstruction. On doing this a carcinoma of the gall bladder with metastases about the liver and pylorus was found. It was clearly an inoperable case—not even the bile ducts could be isolated and drained. The wound was closed. No unusual amount of hemorrhage from the tissues was noticed. The operation produced but little effect on the patient, as she did not even know

that the abdomen had been opened—an undesirable psychical factor being thereby eliminated.

During the first week following the operation and transfusion the patient continued to improve. She looked better and was more cheerful and hopeful. Her appetite increased, her nausea and vomiting disappeared, and on the fourth day after the operation her stools were free from blood for the first time in three weeks. She continued to gain. Twenty-eight days after the transfusion there had been no recurrence of hemorrhage in any part of the body. At this time she had lost no more weight, her appetite was fairly good, there was no bile in the stools, but the urine still contained bile and the jaundice remained about the same. In spite of such marked improvement a gradual steady decline began, and death occurred from cancer seventy-four days after the transfusion. There was no recurrence of the hemorrhages.

Comment.—In this case the pathologic hemorrhage was pronounced, and if an operation had been performed before the transfusion the patient probably would have bled to death. Moreover, in her condition of collapse the operation alone would doubtless have caused death. Both the complete cessation of the hemorrhage and the remarkable revival of the patient were most striking. The carcinoma itself was apparently not affected.

Case No. IX, 14 (6,940). Abstract. Consultation with Dr. M. A. Albl.

Miscarriage at Three Months Three Weeks Before Entrance; Purpuric Condition with Oozing from Vagina, Gums, Posterior Nares, and into Skin; Failure of Treatment; Transfusion; Temporary Arrest of Oozing; Later Hematemesis; Sudden Death Three Days after Transfusion; Autopsy not Permitted.

The patient was an American woman, twenty years of age, with a negative family history. She had had the usual diseases of childhood.

Three weeks previously she had had a miscarriage, after she had been pregnant for three months. No cause for its occurring could

be ascertained. The existence of venereal disease was denied. The bleeding from the vagina was profuse, and from then up to the time of the transfusion she bled constantly from vagina, gums, and posterior nares.

The night that the patient came to the hospital she was very anemic, her skin was saffron-yellow and covered, especially on the extremities, with well-defined petechiæ. The conjunctivæ were yellow. The teeth were discolored and the spaces between them were filled with clotted blood. The blood was pale and watery and the coagulation time was apparently lengthened. The red count was 1,840,000, and the hemoglobin 20 per cent. The pulse rate was 125 per minute and the blood-pressure 80 mm. of mercury. Nothing abnormal was found in the urine. Other treatment having failed, it was decided to transfuse.

The husband of the patient served as donor. One of his radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for fifteen minutes. Before the flow began the patient was bled 250 c.c.

Shortly after the transfusion the patient complained of great pain in the cardiac region. The bleeding from the gums ceased, but recurred twenty-four hours later; the transfusion wound bled. There was considerable vomiting, the vomitus being composed largely of blood.

The following morning the urine was of a reddish-brown color. The guaiac test was negative. No blood smears were made. The patient died rather suddenly two days later. The immediate cause of death could not be determined.

Comment.—This case is an example of the uncertain effect of transfusion when pathological factors exist in the blood. Unfortunately we do not know the true pathology of purpura. In this case the hemorrhage from the superficial points ceased after the transfusion, but it was not determined whether the hemorrhage from the stomach also ceased, and, finally, it was not determined whether death was due to the mixture of fresh blood with pathological or to the natural progress of the disease. It is certain that death was imminent at the time of the transfusion.

Case No. IX, 15 (7,120). Abstract. Consultation with Dr. J. Anderson, Salem, Ohio.

Cholelithiasis; Cholecystectomy; Persistent Jaundice; Appearance of Blood on Dressings Ten Days after Operation; Exploration of Wound; Pathologic Hemorrhage from Cut Surfaces; Transfusion; Disappearance of Symptoms of Hemorrhage; Marked Rise of Pulse Rate by End of Three Hours; Death on Second Day after Transfusion; At Autopsy Abdomen Found to be Filled with Clotted Blood.

The patient was an American woman, thirty-eight years of age, who complained of pain in her right side. Her father died of tuberculosis. There was no history of hemophilia or neoplasm. Except for having had the usual diseases of childhood and grippe fourteen years previously, her personal history was negative.

Sixteen months previously she had had pain in her epigastrium and was jaundiced. Her stools were clay-colored and her urine was dark. She was sick for three weeks. From then up to the time of the operation she had attacks every week of severe pain passing from the epigastrium into the back. In sixteen months she had lost 30 pounds in weight.

When the physical examination was made the patient was found to be rather emaciated. Her sclera were jaundiced, and her entire skin was colored an olive green. The heart was negative and the lungs also, except for a few fine râles in each axilla. The abdomen showed normal outlines. The respiratory movements were rather restricted. Over the epigastrium there was muscular spasm, and also under the right costal margin. The liver edge extended 2 cm. below the costal margin, and was soft. There was no dullness in the flanks. The hemoglobin was 75 per cent.

Through a 10-cm. incision the gall bladder was exposed and opened and several small gallstones removed. The bladder itself was much inflamed and was removed, the edges being brought together with a running catgut suture. The abdominal wound was closed in layers.

On the tenth day after the operation the jaundice still persisted and there was some blood on the dressings. On probing the wound it was found that the stitches had not held, and that there was oozing of blood and serum from all the cut surfaces. The pulse rate then rose from 95 to 150 per minute in three hours, and the patient complained of severe pain over the incision and in the left flank. Her legs were bandaged and the foot of her bed raised. She was in a

cold perspiration. A little later she was taken to the operating room to be transfused.

The husband of the patient served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The blood was allowed to flow across for thirty-eight minutes.

The pulse after the transfusion was much better in quality. The rate had fallen from 144 to 120. The transfusion was ended at 9.05 A.M. The general condition was very much improved.

Three hours later it was noticed that the pulse had risen to 150 per minute and that the patient's face had an anxious expression. Her abdomen was distended. No dullness could be detected. There was no cardiac dilatation, and no evidence of embolism or internal or external hemorrhage could be found. The temperature was only slightly elevated. Pain was present in the left side under the ribs.

Eleven hours after the transfusion the condition was about the same. The temperature was subnormal, the extremities cold, and the abdomen still distended. The hemoglobin was 75 per cent (Tallqvist). There was no air hunger or pain. No indications could be found of embolism, thrombosis, acute cardiac dilatation, pulmonary edema, or hemorrhage. The only conclusion that was reached was that there was an overwhelming intoxication, either from the local septic field following the attempts at arresting the hemorrhage, or from the decomposition of old blood in the intestines, which had not been removed under the usual postoperative laxative treatment.

No further transfusion was performed. Saline infusion and cardiac stimulants were given, and calcium lactate. The legs were bandaged and the feet elevated. Death occurred on the twelfth day after the operation, due to gradual failure of the heart. The patient retained consciousness until near the end.

At the autopsy the abdomen was found to be filled with clots and fresh blood.

Comment.—In this case the transfusion did not arrest the internal hemorrhage.

CASE NO. IX, 16 (7,285). ABSTRACT. CONSULTATION WITH DR. C. E. NORRIS, AKRON, OHIO.

Henoch's Purpura; Blood in Stools, Vomitus, and Urine; Transfusion; General Improvement but Persistence of Slight Hematuria and Purpura One Month Later.

The patient was a child, four years of age. His family gave no history of neoplasm, hemophilia, or purpura. He had had measles, but no other illnesses. He had never had edema of the face or ankles, and his urine had never contained blood.

About two and a half months before entrance he began to complain of soreness and pain in his ankles, knees, legs, and arms. His joints were not red or swollen, but he did not want to have them touched or use them. At the same time reddish spots began to break out on his body. They first appeared on his lip and were only a few in number, but soon increased and spread to his trunk. The largest were the size of a pea, the smallest that of a pinhead. They would come out in the night, stay for two three days, and then fade away only to be replaced by new crops. For a time he was broken out all over except between the umbilicus and chest. For about two weeks he complained of pain. It was variable. Sometimes it would disappear. It usually appeared in the afternoon. Then by the next morning a fresh crop of spots would be out. Two days after the onset of the spots he began to vomit, and for a week could keep nothing on his stomach. Blood was present in the vomitus and in his stools at this time. There was no blood in the urine until two weeks previous to his entrance, and from then on it was present in varying amount. The child's physician said that he had had no fever. He had never had any bleeding from his nose and gums. He had not bled much when cut, but the wounds were slow in healing.

The physical examination showed the patient to be a well-built and fairly nourished boy. He had no edema. His gums were normal. There was no bleeding from his nose. His skin and mucous membranes were somewhat pale. On his forearms, legs, buttocks, and prepuce were numerous reddish and copper-colored spots which varied in size from a pinhead to that of a pea. They were apparently due to the presence of subcutaneous hemorrhages. The edge of the liver could be palpated at the costal margin. Its upper border was at the sixth rib. The edge of the spleen could be palpated just below the costal margin.

Owing to the beneficial effect in other pathologic hemorrhages, it was decided to perform a transfusion. Preliminary hemolysis tests showed that the blood corpuscles of the donor were slightly hemolyzed by the serum of the patient, but that there was no reverse hemolysis or autolysis.

The patient's father served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by

the cannula method. No difficulty was experienced. A preliminary bleeding was not done on account of the amount of blood that had already been lost. The flow was allowed to continue for twelve minutes, but was interrupted in order to avoid acute cardiac dilatation.

At the end of the transfusion the patient's face was flushed. His pulse had fallen from a rate ranging between 138 and 152 per minute to 120 per minute. The blood-pressure was not taken with apparatus, but it was evident that it had risen considerably. The general condition was improved.

The next day there was less blood in the urine, but there were two new larger spots of purpura on the buttocks. The general condition was excellent. On the third day after the transfusion there were a few spots on the legs. Those on the buttocks and forearms were disappearing. The urine was only slightly blood-tinged. At the end of six days both legs were covered with new and old spots which somewhat resembled measles. The urine was still faintly bloody. The joint symptoms had all disappeared. The patient was discharged.

Two weeks after the transfusion a note from the patient's physician, Dr. Norris, stated that he was "thriving wonderfully," and that he still had a slight amount of blood in the urine, and that he had had a very slight purpuric outbreak on one arm since leaving the hospital. A month after the transfusion another note from Dr. Norris stated that the patient weighed 2 pounds more than he ever had before, that he still had a few spots on arms and legs, and also slight hematuria.

Comment.—This case suggests the condition called Henoch's purpura. Osler has described 13 cases of it (Jacobi's *Festschrift*, 1900). As the patient's attack was his first one the question as to possible recurrence cannot be answered until later. The cutaneous lesions were almost entirely those of simple purpura, although at one time the eruption was somewhat papular. In other ways the description clearly tallies with the one which Osler gives of Henoch's purpura. The final outcome is yet to be observed, but at present the patient is apparently well.

Case No. IX, 17 (7,288). Abstract. Consultation with Dr. E. H. Season and Dr. H. J. Lee.

Severe Postpartum Hemorrhage; Normal Expulsion of Placenta; Clots Removed from Uterus; Continuance of Hemorrhage in Spite of Hot Intrauterine Douche and Massage of Uterus; Uterus Packed; 800 c.c. Normal Saline Solution Given Subcutaneously; Slight Temporary Improvement Only; Transfusion; Much Greater Improvement; Uninterrupted Recovery.

The patient was an American woman, thirty-five years of age, who had had a profuse postpartum hemorrhage after her second confinement.

The labor had lasted twenty hours, the child being born at 4 p.m. As the position of the child in the uterus had been that of right occiput to the rear, Dr. Season rotated the head into the right anterior position and delivered with forceps. After the apparently normal expulsion of the placenta, there was a profuse hemorrhage which could not be controlled by kneading the uterus or by giving a hot intrauterine douche. The clots were removed with the hand and a firm gauze packing was inserted. This partly controlled the hemorrhage, although there was still considerable oozing. The patient became extremely weak and was semi-delirious. Eight hundred cubic centimeters of normal saline solution were given subcutaneously with slight improvement.

When the patient was first seen at 8 p.m. she was very pale, restless, semi-delirious, and very thirsty. The pulse was running, of poor volume and tension, and becoming more and more rapid. The respirations were 48 per minute. Over the apex of the heart no second sounds could be heard. The first sounds were barely audible. Transfusion seemed to offer the best chances of relief.

The patient's husband served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The vein was pulled through the cannula and cuffed back, and the artery pulled over the vein. After allowing the blood to flow over for five minutes it was found that the cannula was too large. A smaller cannula was substituted. The total duration of the flow was about thirty-five minutes.

As the blood began to flow across, the patient's blood-pressure rose, the pulse rate fell, the tension improved, and the respiration fell. By the end of the transfusion the pulse was down to 148 per minute. A little later it fell to 120. The respirations fell to 36 at first, and later to 30. The semi-delirium passed away very

rapidly, there was no indication of acute cardiac dilatation, and, in short, a desperate condition was rapidly converted into a favorable one. Just before the transfusion the oozing through the packing had ceased.

The subsequent history was equally favorable. At the end of thirty-six hours the patient was able to nurse her baby. The convalescence was rapid and uninterrupted. The donor felt no ill effects aside from feeling weak for about four days, but this was doubtless due to the great mental strain as well as to the loss of blood.

Comment.—This case shows that transfusion may be performed as an emergency measure with success. The operation was done in a bedroom by the light of a single lamp with only ordinary surgical instruments, aside from the transfusion cannulæ. The struggles of a dying, delirious patient had to be overcome. It was again demonstrated that transfusion may succeed when saline infusion fails.

CASE NO. IX, 18 (7,439). ABSTRACT. CONSULTATION WITH DRS. A. AND B. PESKIND.

Vaginal Hysterectomy for Carcinoma of the Cervix Uteri; Subsequent Severe Hemorrhage from Needle Wounds and Incision; Transfusion and Laparotomy at Same Time; Oozing Controlled with Great Difficulty by Over-and-Over Sutures; Complete Cessation Soon After Flow was Started; Uninterrupted Recovery with no Recurrence of Hemorrhage.

The patient was a German woman, fifty-six years of age, who had cancer of the cervix uteri. Her family and previous history were negative as regards tuberculosis, neoplasm, or hemophilia.

For the past two years she had had repeated hemorrhages from the vagina. The gross appearance of the cervix indicated cancer, and a later histological examination proved it to be present.

A hysterectomy was performed by the vaginal route in the usual way without any unusual incident occurring. All the bleeding points were carefully tied off and all raw edges were obliterated. The patient rallied from the operation fairly well. About an hour after the operation she showed signs of active hemorrhage. Her red count and hemoglobin progressively fell, her white count rose

sharply, she sweated freely, there was shrinkage of the face and marked air-hunger. It was decided to transfuse and perform a laparotomy.

A donor was obtained who was not related to the patient. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. The blood was allowed to flow across for about forty minutes.

The laparotomy was begun while the transfusion was in progress. A large amount of blood was found in the abdominal cavity. The bleeding was from the stitch holes and lines of incision of the previous operation. It was only controlled with the greatest difficulty by sewing over and over, and even then it did not stop until the transfusion had been in progress for some time. The abdomen was flushed out, and enough blood given to restore the patient to a safe condition. The usual immediate stimulating effect was obtained with very marked and satisfactory general improvement. The convalescence was rapid and uninterrupted. There was no evidence of recurrence of the hemorrhage.

Comment.—The oozing in this case simulated that of hemophilia, although from the history it could not be said to be a case of hemophilia unless possibly of the sporadic type. The patient was anemic before the operation. The transfusion not only replaced the blood lost after the operation, but added more than she had had before. In addition, it arrested the tissue oozing.

CASE NO. IX. 19 (7,418). CONSULTATION WITH DR. C. E. NORRIS, AKRON, OHIO.

Essential Renal Hematuria; Nephrotomy without Discovery of Cause of Hemorrhage; Continued Subacute Hemorrhage for Eleven Days; Transfusion Followed by Nephrectomy; Patient in Better Condition than Before Transfusion; Recovery without Recurrence of Hemorrhage.

The patient, a man fifty-one years of age, complained of pain in the right side of his abdomen. Except for the fact that a sister had died of Bright's disease, his family history was negative—there was no history of tuberculosis, neoplasm, or hemophilia. He had never had any previous illnesses except measles when a child, inflammation

of the bowels when twenty-two years of age, and appendicitis and operation two years previously.

For the past three years the patient's appetite had been poor. Since the operation he had had attacks of severe pain which began in the lumbar region and radiated downward. They occurred about once in three months, and were accompanied by vomiting, frequency of micturition, and a desire to defecate frequently. In the eight previous months his urine was frequently examined both before and after the attacks. His physician told him that nothing of consequence was found before, but that afterward red corpuscles, pus, and sometimes casts and albumen were present. A previous X-ray examination had shown nothing. The last attack had occurred a week previously.

The physical examination showed nothing of particular significance beyond the fact that the right kidney was somewhat enlarged and quite tender on palpation. Another X-ray examination showed nothing. A cystoscopic examination was made. It was found that the left ureter could be catheterized easily, but that the catheter could not be inserted into the right ureter. Urine from the left kidney contained occasional red corpuscles, white corpuscles, and small round epithelial cells, but no albumen. No urine could be obtained from the right kidney. Tuberculin was given on two occasions, but caused no reaction. As the patient had another attack of severe colicky pain after the examination, it was decided to operate.

A lumbar incision was made over the right kidney. When the kidney was exposed it was found that the capsule was not adherent, no diseased areas could be seen, no stones could be felt, and nothing abnormal could be detected. A long whalebone bougie was passed through the ureter to the bladder without difficulty. The kidney was split to the pelvis by a longitudinal incision, and still nothing abnormal could be found. It was sewed up by a continuous catgut suture of the interior, and a number of through-and-through sutures, which controlled the hemorrhage well. An incision was then made over the gall bladder, but here again nothing abnormal was found. The patient endured the operations well.

About twenty-four hours after the operations the pulse went up from 98 to 132 in an hour, and the dressings of the lumbar wound became soaked with blood. There was some dullness in the left flank—the side on which the patient was lying. At times there was a great deal of pain, which was probably due to the passage of blood clots through the ureter. The urine contained considerable blood.

For the next nine days the symptoms were about the same—there were still clots and fresh blood in the urine, the patient had complete loss of appetite, and was slightly jaundiced. The lumbar wound had healed by first intention. The blood counts showed that there was a steady and rather rapid diminution of the red corpuscles and the hemoglobin, while the white count was steadily rising. It was decided to transfuse and then perform a nephrectomy.

A son of the patient served as donor. One of his radial arteries was anastomosed to a median basilic vein of the patient by the cannula method. Hemolysis tests had shown no evidence of autolysis, hemolysis, or reverse hemolysis. The blood was allowed to flow across for fifty-five minutes.

While the transfusion was going on the lumbar wound was reopened and enlarged, and the kidney removed without difficulty. By the end of the operation and transfusion the patient was in better condition than when brought to the operating room. With the source of the hemorrhage removed, no more blood appeared in the urine. The convalescence was broken by the occurrence of singultus, which began on the next day and persisted for several days, but it was otherwise uninterrupted. The patient was discharged on the twentieth day after the operation. A careful macroscopic and microscopic examination of the extirpated kidney showed no explanation for the occurrence of the hemorrhages before and after operation.

Comment.—The transfusion well served its purpose in overcoming the symptoms caused by the subacute secondary hemorrhage, and enabled the patient safely to undergo having the source of the hemorrhage removed. Apparently the case was one of "essential" renal hematuria.

Case No. IX, 20 (7,477). Abstract. Consultation with Dr. W. O. Osborn.

Papilloma of Bladder with Carcinomatous Degeneration; Continuous Hematuria; Simultaneous Transfusion and Operation; Removal of Portion of Bladder with the Tumor; Patient in Better Condition than Before Operation; Recovery.

The patient was an Englishman, fifty-four years of age, who complained of having blood in his urine. His family history was negative as far as it was known. He had had rheumatic and

typhoid fevers twenty-six and thirty-six years previously, respectively.

For more than a year he had noticed increasing frequency of micturition, hematuria, and pain in his bladder. The hematuria had persisted in spite of local treatment. He had lost considerable strength and weight and was markedly anemic.

Dr. Lower made a cystoscopic examination and reported the presence of a large papilloma which he believed had undergone malignant degeneration. The tumor seemed to be localized, and on examination by rectum seemed to be confined to the bladder wall. At this time the patient was confined to his bed, his pulse ranged from 120 to 140, his blood-pressure from 110 to 120, his red count was 1,900,000, and his hemoglobin 30 per cent. With the progressive hematuria and the gradual decrease in strength, an operation seemed to be urgently demanded, but his condition was such that he was obviously a poor surgical risk. Therefore it was planned to transfuse and operate at the same time.

A son of the patient served as donor. One of his radial arteries was anastomosed to a superficial vein near the elbow of the patient by the cannula method. The blood was allowed to flow across a total length of time of thirty-two minutes, although the flow was interrupted as occasion demanded.

After a short time the patient was anesthetized while the transfusion proceeded, a suprapubic incision was made and a large part of the bladder which bore the tumor was removed. The ureter was involved, and an extensive dissection was required to free it. At the beginning of the transfusion his pulse was 138, his blood-pressure 110 mm., and his face pale. At the end of the transfusion his pulse had fallen to 104, the blood-pressure had risen to 132 mm., and his entire face was pink. There was no further hemorrhage, no evidence of shock, and the general condition was much better than before the operation. A good recovery followed. The pathologist reported the tumor to be a papilloma undergoing carcinomatous degeneration.

Comment.—This case corroborated the laboratory observations, viz.: that by transfusion a poor surgical risk may be converted into a good one, at least under certain conditions. Not only was the operative shock wholly combatted, but the patient left the table in better condition than he was in before. During the operation blood was added as needed.

SUMMARY

Case No. IX, 1 (6,411).

First Transfusion:

Transfused.—For acute postoperative renal hemorrhage.

Immediate Result.—Enough relief afforded to permit immediate nephrectomy.

Other Treatment.—Nephrectomy.

Late Result.—Recovery from operation. Acute pathologic hemorrhage from bladder wall at end of two weeks.

Second Transfusion:

Transfused.—For acute pathologic hemorrhage from bladder wall.

Immediate Result.—Cessation of hemorrhage, and relief from symptoms caused by loss of blood.

Other Treatment.—None.

Late Result.—No recurrence of hemorrhage in twenty months. Complete recovery.

Case No. IX, 2 (6,852).

Transfused.—For acute hemorrhage from uterus.

Immediate Result.—Enough relief afforded to permit elimination of source of hemorrhage.

Other Treatment.—Curettage, hysterectomy for adenocarcinoma.

Late Result.—Patient well, and with no known recurrence of growth in twelve months.

Case No. IX, 3 (7,110).

Transfused.—For acute hemorrhage from mesoappendiceal artery after appendectomy.

Immediate Result.—Symptoms of hemorrhage eliminated.

Other Treatment.—Ligation of artery.

Late Result.—Death on third day from acute infection.

CASE NO. IX, 4 (6,492).

Transfused.—For acute intestinal hemorrhage in typhoid fever.

Immediate Result.—Marked improvement in general condition.

Other Treatment.—None.

Late Result.—Continued hemorrhages; death on seventh day.

CASE NO. IX, 5 (6,539).

Transfused.—For acute intestinal hemorrhage in typhoid fever in a patient *in extremis*.

Immediate Result.—Complete resuscitation.

Other Treatment.—None.

Late Result.—Continued hemorrhages; death on third day.

CASE NO. IX, 6 (6,408).

Transfused.—For secondary hemorrhage following nephrotomy for calculus.

Immediate Result.—Elimination of symptoms; cessation of hemorrhage.

Other Treatment.—None.

Late Result.—Death from peritonitis (not connected with transfusion) on tenth day.

CASE NO. IX, 7 (6,540).

Transfused.—For chronic hemorrhages from bowels.

Immediate Result.—Cessation of hemorrhages; elimination of symptoms.

Other Treatment.—Suturing of rectal ulcers at end of three weeks, at which time there was slight bleeding.

Late Result.—No recurrence of bleeding in twenty-seven months; complete recovery.

Case No. IX, 8 (6,854 and 6,957).

First Transfusion:

Transfused.—For chronic hemorrhage from bowels.

Immediate Result.—Slight improvement only.

Other Treatment.—None.

Late Result.—Persistence of condition with some improvement at end of three months.

Second Transfusion:

Transfused.—For same condition.

Immediate Result.—Immediate diminution of amount of blood in stools.

Other Treatment.—None.

Late Result.—Disappearance of blood at end of four weeks; no blood at end of nine weeks.

Case No. IX, 9 (6,663).

Transfused.—For hemorrhage from bowels of tuberculous origin.

Immediate Result.—Gradual cessation of hemorrhage.

Other Treatment.—None.

Late Result.—Occasional trace of blood and slight mucous colitis at end of sixteen months.

Case No. IX, 10 (6,633).

Transfused.—For hemorrhage from bowels.

Immediate Result.—Cessation of hemorrhage.

Other Treatment.—None.

Late Result.—No recurrence at end of twenty-five months.

Case No. IX, 11 (6,538).

Transfused.—For hemorrhage from bowels.

Immediate Result.—Cessation of hemorrhage.

Other Treatment.—None.

Late Result.—No recurrence at end of eighteen months.

Case No. IX, 12 (6,605).

Transfused.—For subacute hemorrhage from the kidney of "essential" origin.

Immediate Result.—Elimination of symptoms of hemorrhage so that nephrectomy could be performed; no effect on bleeding in two days.

Other Treatment.—Nephrectomy.

Late Result.—Complete recovery.

Case No. IX, 13 (6,537).

Transfused.—For acute pathologic hemorrhages associated with icterus.

Immediate Result.—Complete cessation of hemorrhages.

Other Treatment.—Exploratory laparotomy for diagnosis.

Late Result.—Death from carcinoma of gall bladder after seventy-four days; no recurrence of hemorrhage.

Case No. IX, 14 (6,940).

Transfused.—For purpura three weeks after a miscarriage.

Immediate Result.—Temporary arrest of oozing, but development of bleeding from stomach.

Other Treatment.—None.

Late Result.—Death at end of two days with continued oozing; cause of death undetermined.

Case No. IX, 15 (7,120).

Transfused.—For acute hemorrhage following cholecystectomy, and associated with icterus.

Immediate Result.—Elimination of symptoms of acute hemorrhage; failure to arrest hemorrhage.

Other Treatment.—Saline infusion, calcium lactate internally.

Late Result.—Death on second day after transfusion.

Case No. IX, 16 (7,285).

Transfused.—For pathologic hemorrhage occurring in "Henoch's purpura."

Immediate Result.—Marked general improvement and diminution of the hemorrhages.

Other Treatment.—None.

Late Result.—One month after transfusion slight hematuria still persisted, and a few purpuric spots on the arms and legs. The patient weighed more by 2 pounds than he had ever weighed before.

Case No. IX, 17 (7,288).

Transfused.—For severe postpartum hemorrhage.

Immediate Result.—Elimination of symptoms of hemorrhage.

Other Treatment.—Eight hundred cubic centimeters of normal saline infusion gave only slight relief before the transfusion.

Late Result.—Uninterrupted recovery.

Case No. IX, 18 (7,439).

Transfused.—For severe pathologic hemorrhage subsequent to vaginal hysterectomy for carcinoma of the cervix uteri.

Immediate Result.—Elimination of symptoms of hemorrhage; cessation of the pathologic hemorrhage.

Other Treatment.—None.

Late Result.—Uninterrupted convalescence; no return of hemorrhage; recurrence of carcinoma to be determined.

Case No. IX, 19 (7,418).

Transfused.—For continuous subacute hemorrhage subsequent to exploratory nephrotomy ("essential" renal hematuria).

Immediate Result.—Symptoms of hemorrhage eliminated so that nephrectomy could be performed.

Other Treatment.—Nephrectomy.

Late Result.—Uninterrupted recovery.

CASE NO. IX, 20 (7,477).

Transfused.—For hemorrhage from a papilloma of the bladder which had undergone carcinomatous degeneration, and to prevent shock.

Immediate Result.—Patient in better condition than before the operation; no shock.

Other Treatment.—Removal of a portion of the bladder and the tumor.

Late Result.—Recovery.

Other cases in which hemorrhage was present are I, 2 (6,706) and VIII, 7 (6,895).

CASES FROM OTHER SOURCES

CASE A. MOSLER.

Acute Hemorrhages from Bowels in Typhoid Fever; Transfusion; Cessation of Hemorrhages; Recovery.

The patient was a woman, thirty-seven years of age, who had typhoid fever. Late in its course she had hemorrhages from the bowels, and lost about 1¼ quarts of blood with consequent collapse—her pulse was 130 per minute, her face pinched, the respirations shallow and rapid, the extremities cold, and she lay in a somnolent condition. She rapidly grew worse, in spite of different remedies being used. Transfusion was finally undertaken as a last resort. About 120 gms. of defibrinated human blood were injected into her radial artery. At the end of half an hour she had a severe chill which lasted for eight minutes. Improvement began at once. There was no recurrence of the hemorrhage. Convalescence was only interrupted by the formation of a carbuncle on the lower part of the back.

Case B. Stone.

Acute Hemorrhages from Bowels in Typhoid Fever; Transfusion; Cessation of Hemorrhages; Recovery.

The patient was a male, twenty-three years of age, who began to have hemorrhages from the bowels at about the eleventh day in the course of typhoid fever. They continued at irregular intervals until the eighteenth day, when he lost a large amount of blood and passed into a state of collapse with a subnormal temperature of 96.5° F., a pulse rate of 150 per minute, and colorless skin and mucous membranes. On the twentieth day transfusion seemed to offer the only chance of recovery. From 12 to 16 ounces of blood were taken from a sister of the patient and injected into his median basilic vein (whether the blood was whole or defibrinated is not stated). At the time of the transfusion, the pulse was 130 and very weak. After the transfusion the patient immediately felt better, and the pulse rate fell to 120 and was of much better quality. The fever continued for four weeks longer, but no further hemorrhages occurred. Before the transfusion attempts were made to arrest the hemorrhages with ergot, opium, lead, persulphate of iron, gallic acid, turpentine, and other so-called hemostatics, but with no result.

Case C. Gibert.

Acute Hemorrhages from Bowels in Typhoid Fever; Transfusion; Recovery.

The patient had typhoid fever with no special symptoms appearing until the thirty-first day, when he passed into a state of collapse with the appearance of a small amount of blood in the stool. This was followed by a condition of great excitement in which he got out of bed. In the struggle incident to putting him back he passed about 1,500 gms. of blood by rectum. Delirium ensued immediately, and such weakness that from 25 to 30 gms. of blood were transfused. There was slight improvement, and a second injection of 90 gms. was made the following morning (the exact method of performing the transfusion, and whether whole or defibrinated blood was used, is not stated, although it was probably the latter, as the statement was made that it was injected). There was immediate, rapid, and permanent improvement, the brain being the first to show the results. The heart beat normally, the first sound became perceptible, the cardiac impulse was felt, the patient came out of his

death struggle and was able to be nourished. Convalescence set in at once and recovery was uninterrupted. Presumably there was no further hemorrhage from the bowels, although the definite statement is not made.

Case D. Whitwell.

Acute Hemorrhages from the Bowels in Typhoid Fever; Infusion of 15 Ounces of Saline Solution; Aggravation of Condition; Transfusion; Recovery.

The patient was a male, thirty-two years of age, who had repeated hemorrhages from the bowels early in the fourth week of the disease. On the day on which the transfusion was done, it was estimated that he lost 18 ounces of blood, and this, added to his previous serious condition, reduced him to a state of extreme collapse. At first an intravenous saline infusion of 15 ounces was given. His condition immediately became worse, and did not improve in spite of the infusion and vigorous stimulation. Five and a half hours after this 6 ounces of whole blood were injected intravenously from the arm of the nurse into the patient in two minutes. The distress was great and the breathing rapid, but the pulse remained about the same. Ergotin and black coffee were also given. Within four hours there was improvement. By the end of eight hours it was very great, and the body became dry and warm for the first time in eighteen hours. Ergotin was injected for a week after the transfusion. There was but one bloody stool (on the second day after the transfusion) and recovery was uninterrupted.

Case E. Haveman (Darène).

Acute Hemorrhage from the Bowels in Typhoid Fever; Transfusion; Recovery.

A girl, eighteen years of age, had a violent intestinal hemorrhage after about two weeks had elapsed in an attack of typhoid fever. The loss of blood was calculated to be about 3 pounds. She was in such a state of collapse as a result that it was decided to transfuse, although there was apparently little chance of her recovering. About 6 ounces of defibrinated human blood were injected into the peripheral end of the radial artery. The symptoms of collapse disappeared at once, and, while the usual chill occurred, a complete cure resulted.

Case F. Bern, Kussmal, Czerny (Darène).

Acute Hemorrhages from the Bowels in Typhoid Fever; Transfusion; Further Hemorrhage; Death.

The patient was a male who had a profuse intestinal hemorrhage in the course of an attack of typhoid fever. To combat it 150 gms. of defibrinated human blood were injected into his veins. At the beginning of the transfusion there were no threatening symptoms. Half an hour after it was over he was seized with violent chills. During the transfusion rumblings in the abdomen were heard which were supposed to be due to the transfusion of too large an amount of blood, causing increase in the peristalsis. Two hours after the transfusion he had another hemorrhage and lost a large amount of liquid red blood. He became gradually exsanguinated and died in collapse. There was no autopsy.

Case G. Spillman (Darène).

Acute Hemorrhages from Bowels in Typhoid Fever; Transfusion; Further Hemorrhage; Death; Autopsy.

The patient was a male, twenty-eight years of age, with typhoid fever, who had repeated intestinal hemorrhages. When death seemed imminent 150 gms. of defibrinated human blood were injected into his veins. At the expiration of some minutes a chill developed which lasted nearly two hours. The pulse was improved, and the patient replied more clearly than he previously had to questions which were addressed to him. The next morning the pulse was regular and 104 per minute. However, during the day the hemorrhage recurred and the patient died. At the autopsy ulcerated Peyer's patches were found covered with gangrenous flaps, some of which were detached. The heart was large and showed fatty infiltration. The kidneys were altered.

Case H. Roussell (Darène).

Subacute Hemorrhages from the Bowels, following Typhoid Fever; Probable Double Pneumonia; Transfusion; Intestinal Perforation Ten Hours Later; Death; Autopsy.

The patient was a girl, fifteen years of age, who had had, since November 4, 1873, Caucasian fever followed by typhoid fever, with three relapses. The intestines were ulcerated, and she had a passive bloody diarrhea with 17 to 20 movements a day. When seen in

March, 1874, she was in the last degree of anemia, had bedsores, fainting spells, and signs of double pneumonia—rapid respiration, bloody sputum, etc. Transfusion was undertaken as a last resort, and 140 gms. of whole human blood were slowly injected into her veins. Half an hour later the pulse was better, the respiration was good, she was sleepy, and she had a marked chill. Two hours later she had the first solid stool free from blood which she had had for a long time. After a fairly good night, and ten and a half hours after the transfusion, she had all the symptoms of intestinal perforation—sudden very violent pain in the abdomen, vomiting, a drawn face, and the sudden development of tympanites—and death occurred. At the autopsy pus and fetid matter were found in the abdominal cavity and two small perforations in a Peyer's patch. There was no trace of a clot in the vein of the arm operated on, and the urine contained no albumen or blood.

Case I. Mahomed.

Acute Hemorrhages from the Bowels in a Relapse from Typhoid Fever; Transfusion; Further Hemorrhages Six Days Later; Death on Ninth Day after Transfusion.

The patient was a male, twenty-six years of age, who had typhoid fever and suffered from a relapse. On the tenth day of the relapse and the thirty-fifth of the fever he had a severe hemorrhage, which recurred twice on the following day. He was exhausted, anemic, had cold extremities, and was restless. His pulse was 160 per minute, very small, thready, and often irregular. He was evidently fast sinking when transfusion was performed (by what method, or whether defibrinated or whole blood was used, was not stated). The immediate result was to bring the pulse down from 160 to 144. The patient rallied for a few days and gained enough ground to give hopes of his ultimate recovery. Six days after the transfusion there was another small hemorrhage, which caused a sudden change for the worse. Then one or two more slight losses of blood soon reduced him to a state of exhaustion from which he did not recover. Death occurred on the ninth day after the transfusion.

Case J. Mahomed.

Acute Hemorrhages from the Bowels in Typhoid Fever; Transfusion *In Extremis*; Improvement for Two Days; Death from Pulmonary Complication on the Fifth Day after Transfusion.

The patient was a male, twenty-five years of age, with typhoid fever, "who, during his attacks of fever, suffered a probably irrecoverable injury by collapse of a large part of his right lung, while in addition to this he had severe general bronchitis." On the fifth day after the relapse occurred, and on the thirty-first day of his illness he had a severe hemorrhage. Four days later he had three more severe hemorrhages, and lapsed into a state of complete exhaustion and impending dissolution. On the following day, when he appeared to be *in extremis*, 4 ounces of human blood were transfused "with the best possible effects." For two days the patient rallied greatly. Then his bronchitis increased, and he died from the lung complication on the fifth day after the transfusion.

CASE K. PEPPER AND NISBET.

Hemorrhagic Disease of Unknown Etiology; Bleeding from Gums; Absence of Blood from Urine; First Transfusion; Almost Complete Cessation of Bleeding from Gums; General Improvement; Slight Reddish Discoloration of Urine, Suggesting Hemolysis; Second Transfusion; Marked Hemolysis; Death on Fifth Day after First Transfusion (Third Day after Second Transfusion); Autopsy.

The patient was a male, thirty-three years of age, who complained of bleeding from his gums, which had continued intermittently for ten weeks preceding his admission to the Hospital of the University of Pennsylvania. It gradually increased in severity during this time, so that, for the last four days before admission, on April 16, 1907, it was constant. The physical examination showed that he was in a state of profound anemia, the red cells numbering 970,000 per cubic millimeter, and the white cells 3,600, while the hemoglobin was 20 per cent. The urine at this time contained no red cells, but they were found in the hard, dark, tarry stools on microscopic examination. The conclusion reached in regard to the diagnosis was that the patient was suffering from some obscure type of hemorrhagic disease of unknown etiology; it was decided that the condition was not hemophilia, scurvy, pernicious anemia, or acute leukemia. On April 24th 2,000 units of diphtheria antitoxin were injected in the hope of influencing a possibly undiscovered infection, but the condition grew steadily worse. On April 26th it was decided to perform a transfusion.

On the day of the transfusion the bleeding from the gums was continuous, nausea was present in high degree, tinnitus aurium was

very severe, and the patient seemed to be sinking rapidly. The transfusion was performed by Drs. C. H. Frazier and J. E. Sweet by direct anastomosis of the left radial artery of the patient's wife with a large vein at the left elbow of the patient. The blood was allowed to flow across for one hour and thirty-three minutes. Immediately before the transfusion the blood examined showed 420,000 red cells, 4,200 white cells, and 12 per cent of hemoglobin. Ten minutes before the transfusion ended the red cells numbered 1,001,000, and the hemoglobin had risen to 21 per cent. The subsequent history was as follows:

"April 27th. Patient passed a fair night. Bleeding from gums almost entirely ceased after transfusion and did not recur. Tinnitus aurium entirely ceased in one ear, and was better in the other. Had not vomited since transfusion. Color a great deal better. No jaundice noted.

"April 28th. Patient continued to feel stronger and much better. Bleeding from gums was merely a trace. Stomach not very retentive. At 5.35 P.M. a vein was exposed in the upper left arm by Dr. Frazier. This was found not suitable to the left radial artery of patient's brother-in-law, which was being exposed at the same time. Another vein was exposed in patient's lower arm, and an arteriovenous anastomosis done by Dr. Sweet. Blood was allowed to transfuse from 6.33 P.M. to 7.37 P.M. (one hour and four minutes). Patient reddened visibly during operation. . . . Later in the evening patient lay in a flushed, warm, lethargic condition, probably influenced somewhat by morphin given at operation. Much sweating. No jaundice by artificial light. Temperature 102° F.

"April 29th. Patient this morning was very jaundiced. Stomach had not been retentive since operation. Expectorates green mucoid material from throat. No bleeding from gums. Temperature rose in the afternoon to 104° F. Arm somewhat painful and swollen. Hand edematous. No pus in wounds. Spleen palpable. Urine contained urobilin, hemoglobin, some free blood, and many casts. Blood-pressure, 115.

"After the first transfusion (wife's blood) the urine showed slight reddish discoloration and slight amount of urobilin, suggesting hemolysis, but this had nearly disappeared when the second transfusion (brother-in-law's blood) was undertaken. During the night after this second transfusion the urine changed to a markedly bloody character and subsequently showed a direct proportional relation with the jaundice, oppression, and other evidences of hemolysis.

"April 30th. Passed a poor night. Jaundice worse. Stomach

still not retentive. Temperature still high. Arm condition the same. Mouth very dry, but no bleeding.

"May 1st. Was in a very low state. Blood-pressure, 105. The patient sank rapidly and died May 3, 1907.

"*Autopsy Notes.*—The autopsy was performed by Dr. Pepper on the afternoon of May 4, 1907, the body having been injected with some preservative fluid containing formalin by the undertaker some hours previously. Body of a well-nourished male, extremely anemic in appearance, and exhibiting a fairly intense jaundiced hue of the skin. Subcutaneous fat a bright lemon color. Muscles of the abdominal wall very pale. Numerous easily broken-down but fairly extensive pleural adhesions throughout the left pleura; no adhesions on the right side. The heart was large, both auricles being very much dilated; the heart was empty, and had evidently been injected with formalin, as the walls felt like leather; the right ventricle was dilated. All the valves were normal.

"Both lungs showed small, subpleural hemorrhages, and on section both were riddled with numerous dark-red firm areas, between which the lung tissue was apparently normal and crepitant. The lungs were very dry, and these small areas or nodules were undoubtedly hemorrhagic, and were so firm that they could be palpated throughout the whole lung. Most of them were about the size of a split pea; a few seemed to have coalesced.

"The spleen was normal in size and appearance; on section it was also normal in appearance. The liver was fairly large, smooth, light in color, and on section showed no macroscopic evidence of necrosis; it appeared slightly fatty, but otherwise perfectly normal. The gall bladder contained a small amount of bile.

"The left kidney was large, thick, fairly firm, and rounded; there were a number of small subcapsular hemorrhages. The capsule stripped readily, leaving no trace of the hemorrhages on the kidney. Section of the kidney showed a cortex of normal width; there was no congestion. The parenchyma was clouded and granular in appearance. The right kidney showed exactly the same condition, and in addition an area of hemorrhage in the parenchyma about a centimeter in length. The pancreas was normal. The right suprarenal was normal. The stomach contained a small amount of dark-brown liquid. The mucous membrane was not ulcerated, but was merely dotted here and there with a number of small reddish spots. There did not seem to be any break in the continuity of the mucous membrane at these points. The mesenteric lymph glands were normal in size and appearance. The intestines were not opened. The bone

marrow from the middle of the shaft of the right tibia was normal in appearance.

"*Pathologic Diagnosis.*—Severe anemia. Jaundice. Numerous small intrapulmonary hemorrhages. Dilatation of the heart. Acute parenchymatous nephritis with subcapsular ecchymoses.

"*Microscopic Examination of Tissues.*—Lungs: Hemorrhagic extravasation into alveoli, congestion, and edema. Number of large epithelial cells containing pigment (Hertzfehlerzellen). Kidneys: For most part the epithelium of the tubules presented normal characteristics. In some areas, chiefly in the convoluted tubules, the epithelium was granular, the demarcation between cells obscure, and the nuclei invisible. The lumen of a number of these tubules were filled with granular débris; many others were filled with red corpuscles, more or less disintegrated. Glomeruli presented no unusual features. Proportion between interstitial and parenchymatous tissue was normal. In small scattered areas were found bodies presenting the characteristics of emboli composed of bacteria, but unattended by any inflammatory reaction. Liver: Some deposits of pigment, probably blood pigment, in the liver. (No areas of necrosis.) Suprarenal: Moderate congestion. Pancreas, spleen, and bone marrow normal."

The endeavor was made to determine if the blood serum of the patient was hemolytic to normal red corpuscles. "Sterile blood was collected from the patient eighteen and thirty-six hours after the second transfusion. The blood was allowed to coagulate and the serum used for the following tests: A 5 per cent suspension of washed normal red blood corpuscles in 0.85 sodium chlorid solution was prepared. The serum of the patient was mixed with the suspension of corpuscles in varying proportions. The mixture of serum and corpuscles was kept in an incubator at 37° C. (98.6° F.) for two hours. On removal no evidence of hemolysis was observed. The result was also negative after the incubated mixture had been kept on ice for twenty-four hours. The mixture when prepared as above, and an activating substance supplied by adding normal serum, also failed to show hemolysis."

Comment.—This case presents an additional note of warning in transfusion in certain pathologic states of the blood. Much more exact knowledge is needed before normal blood may be mixed with pathologic blood in certain diseases.

This case is a most interesting and valuable contribution

to the study of transfusion. It is of particular value by reason of the thoroughness with which the authors and their collaborators have studied it in its different bearings.

Case L. Stokes.

Hemorrhages from Nose, Gums, and into Skin in Typhoid Fever; Hematuria; Transfusion; Nosebleed on Second Day; No Further Hemorrhage; Recovery.

The patient was a boy, nine years of age, who had had typhoid fever for about four weeks, when he had hemorrhages from the nose and gums, and every passage of urine had, as far as could be judged, from 2 to 5 ounces of blood in it. The next few days saw the hemorrhages continue, and finally it was evident that death would occur unless they could be stopped. Numerous petechiæ appeared on the neck, arms, and feet. Tonics and astringents failed to produce any results, and transfusion was undertaken. Two and a half ounces of defibrinated blood from the father were injected into the median vein. The next urine passed was entirely free from blood (it was passed within an hour), and no albumin was found in the urine. The second day after the transfusion the patient had a nosebleed, which was controlled by a spray of Monsell's solution. From this time on a marked improvement was begun, and recovery was considered to be complete at the end of three weeks.

" The very sudden stoppage of the hemorrhage from the oozing surfaces was truly remarkable. From the time of introduction of the blood, the oozing from the gums and nostrils stopped absolutely . . ."

Case M. Boisnot.

Purpuric Condition (Hemophilia?); Severe Tissue Hemorrhages; Failure of Treatment; Transfusion; Violent Epistaxis on Third Day; Recovery.

" During the night of June 4, 1874, I was called to see M. H., aged seven years; he had been for some time previous subject to troublesome epistaxis, etc. Both of the child's parents are in good health as well as circumstances, so that the child had had excellent hygienic care. There are four children, the patient being the third in order of birth, and, with him excepted, all are in good health. There was at the time of my visit an intense general pallor, extend-

ing to the lips and internal surface of the eyelids, giving the patient a waxy appearance and making more apparent the existing ecchymotic spots; these last were situated behind the ears, at the angle of the mouth, the roof of the mouth, and a large one of six inches in diameter over the region of the liver. Blood was noticed oozing from the nose, gums, and pharynx, while the quantity vomited led me to infer that there might also be internal bleeding. The pulse was feeble, quick, and rapid; the respiration labored, the tongue pale, moist, and clean. The general expression of the face was anxious to a degree which might call for the term 'frightened.' The hemorrhage at this time was from the nose, and was sufficient to require applications for relief to both anterior and posterior nares."

In spite of dietetic and remedial treatment, the condition was steadily aggravated until eighteen days after the time when the patient was first seen. At that time the condition was critical in the extreme—pulse of 160 and of feeble quality; body surface cool; panting respiration, and general lassitude with a disposition to drowsiness which amounted almost to stupor. Four ounces of blood were taken from the child's father and defibrinated and injected by means of a syringe. "This yielded a result far beyond our most sanguine expectations; in short, recovery began from that day, progressed, and, at this writing, November 2d (three months after the transfusion), is established. It is proper to state that on the third day following the transfusion violent epistaxis recurred. This was arrested by plugging the nares with the aid of Bellocq's cannula." There was no internal medication except quinin and a general tonic.

Case N. Lane.

Hemophilia; Hemorrhage for Six Days after Operation for Squint; Patient in Critical Condition; Transfusion; Recovery; No Recurrence of Hemorrhage in More than Three Weeks; Later Condition not Reported.

The patient was a boy, eleven years of age, who was operated on for squint by Dieffenbach's method. After the operation and the occurrence of the subsequent hemorrhage, it was learned that he had had previous attacks of severe hemorrhage, which followed trifling injuries, and that, on one occasion, he had entered a hospital for an injury of the knee joint, for which leeches were applied with resulting great difficulty in controlling the bleeding from the leech

bites. Shortly after the operation he began to bleed, and kept on bleeding for six days, when his condition was most critical—he was in a state of coma, the radial pulse was imperceptible, his body was cold, etc. On the sixth day 5½ ounces of whole blood from a young woman were injected into his veins by means of a syringe. The only immediate effect reported was the rendering of the pulse perceptible, but in a couple of hours he was able to sit up, and his condition was very much improved. From this time on recovery was uninterrupted, and at the end of more than three weeks there had been no recurrence of the hemorrhage.

Case O. Watts (II).

Gallstones; Jaundice; Operation; Severe Postoperative Tissue Hemorrhage; Patient in Alarming Condition; Transfusion; Temporary Improvement; Continuation of Hemorrhage; Death Five Hours Later; More than 500 c.c. of Blood Found in Abdominal Cavity.

The patient was a woman, forty-one years of age, who was operated on for gallstones with removal of several from the gall bladder and common duct. She had been jaundiced for ten weeks before entering the hospital. The coagulation time of her blood was twelve and a half minutes. A few hours after the operation she began to show signs of hemorrhage, which in six hours became alarming. She was pale, perspired profusely, and the pulse was 140 per minute and very weak. The dressings were saturated with blood. When these were removed considerable oozing could be seen around the gauze drain. The wound was packed tightly with gauze, a tight binder applied to the abdomen, the legs bandaged, and subcutaneous infusions of saline solution and other stimulants administered. In spite of this treatment her condition steadily became worse, and ten hours after the operation it was so critical that it was decided to perform a transfusion. An immediate anastomosis was made between the radial artery of a donor and the median basilic vein of the patient, and the blood allowed to flow across for about one hour and fifty minutes. It was estimated that between 700 and 800 c.c. of blood passed over. During the transfusion the condition of the recipient improved somewhat, but not as much as was hoped. After the operation she seemed brighter, said she felt better, her color was distinctly better, and her pulse was stronger, but still quite rapid (140 per minute). The improvement lasted only a short time. The hemorrhage continued, and she died five hours after the

transfusion was completed. The abdominal wound was opened and the abdominal cavity was found to contain more than 500 c.c. of blood.

Case P. Michel.

Hemorrhage from the Stomach; Patient in Critical Condition; Transfusion; Cessation of Hemorrhage; Disappearance of Blood from Stools at End of Nine Days; Patient Discharged as Being Well.

The patient was a male, sixty-three years of age, who suffered from symptoms apparently of gastric origin. He had previously had diarrhea with black stools and periods of unconsciousness which he characterized as "cramp attacks." The physical examination showed great weakness, yawning, nausea, and tenderness in the epigastrium. Immediately after the examination he vomited three large blood clots and about a pint of fresh blood. It was considered that the bleeding was from a chronic gastric ulcer or from erosion of an atheromatous vessel. The convulsions continued, and more blood was lost from time to time until the patient was in a critical condition. Five days after the examination about 45 c.c. of defibrinated human blood were injected intravenously. An hour later the patient had a severe chill which lasted for half an hour, and which was followed by warmth and sweating. The general condition was improved. There were no more convulsions. There were two more black stools, and others which showed smaller amounts of blood. Nine days after the transfusion the stools were normal in appearance and the patient was discharged as well.

Case Q. Brewer and Carrel.[1]

Melena Neonatorum; Transfusion; Recovery.

"The baby was born of healthy parents, and was delivered after a ten-hour labor by an easy low forceps operation at 5 A.M. on March 4th. The child was a girl and appeared to be healthy, weighed 8 pounds and 12 ounces, breathed and cried at once, and showed no signs of asphyxia. The blades of the forceps made slight marks over the right zygoma and behind the left ear; there was no abrasion of the skin. Five hours after birth the cord was retied because of slight oozing from the cut end. Twelve hours after birth a thickened, dark-colored spot was noticed on the right

---

[1] From a private communication from Dr. Geo. E. Brewer.

side of the tongue which was thought to be a nevus, but which has cleared up since, and was undoubtedly a hematoma. Three hours later the baby's temperature was 102.2° F., and it was put to the breast for the first time. After a quiet night the baby's morning temperature was 102°. She looked pale, and a slight amount of blood was noticed when the mouth was washed. She slept quietly all that morning, but became restless in the afternoon, her temperature at 4 P.M. being 103.4°. She grew markedly paler, cried continuously, and began to bleed slowly but steadily from the nose, and a hematoma appeared in the scalp behind the left ear. At 9 P.M. this subcutaneous bleeding had extended down the neck over the muscles, across the median line to the other ear, across the coronal suture over the frontal bone, and forward under the left ear to the angle of the jaw. The bleeding from the nose was continuous and quite profuse. The temperature was 102.3°, a dark meconium stool gave a very positive reaction for blood, but the urine was of normal color. The baby was of waxen pallor. The diagnosis of melena was made, and treatment instituted on the theory of its being an intestinal infection. One dose of 30 minims of castor oil was given, and 2-grain doses of calcium lactate every two hours during the night.

"During March 6th the child did not seem to grow worse so rapidly. The scalp hematoma increased in size, and tenseness and pallor of the skin increased, but the temperature gradually fell from the maximum of the attack at 2 P.M. (104.4°) until it reached 97.4° at 3 P.M., the nasal bleeding became less constant, and the baby nursed regularly. In the evening of March 6th and during March 7th there was some vomiting of watery fluid containing partially digested blood, especially after taking the calcium lactate. The calcium lactate was stopped. Adrenalin was tried in the nose at this time, but without effect. The feeding had to be done with a dropper, for the baby refused to nurse. The temperature range was 97.8° to 99.4°.

"On the morning of March 8th the case seemed hopeless. During this day the baby's skin was waxen white and the mucous membranes without color; the nasal bleeding was continuous; the vomited matter contained milk curds, dark blood, and at times bright clots; the stools were frequent and contained bright red blood; the subcutaneous hematoma on the scalp increased until the right eye was closed, and ecchymotic spots appeared on the legs; the respiration was rapid and superficial; the pulse weak, 150 to the minute just before the operative procedures.

"It was decided to attempt a direct transfusion of blood from the father of the infant by end-to-end anastomosis of two blood-vessels after the manner devised by Dr. Carrel, of the Rockefeller Institute. This was done by Dr. Carrel and Dr. Brewer. The right popliteal vein of the baby was sutured to the left radial artery of the child's father without anesthetic to either patient, and enough blood was allowed to flow into the baby to change her skin from a pale transparent whiteness to a brilliant red color. No measure of the amount of blood was possible, but the evidences of a sufficient quantity were manifold. She began to cry lustily and to struggle against the bandages which held her strapped to an ironing board. The wound in the leg up to this time had oozed a slight amount of pale watery blood which did not clot well. It began to bleed freely and the blood promptly clotted. The nosebleed stopped instantly. The pulse became full and strong and slowed down, and the respirations were deep and full. As soon as the wound was sutured and dressed the baby was fed an ounce of milk which she took ravenously and retained, and immediately went to sleep.

"Since the ending of the transfusion there has been no hemorrhage, no vomiting, and no diarrhea. Convalescence from the operation was uninterrupted except for a slight infection of the wound. There was no evidence of hemolytic action at any time, and all the symptoms of melena ceased at once. The next morning the baby was found to be 14 ounces below her birth weight. She has gained steadily since, and now, eight weeks after birth, she weighs 10 pounds 15 ounces. The hematoma was absorbed rapidly except for a slight discoloration of the upper lid of the right eye, which still persists. The stools became of normal character two days after the operation. The wound is healed, and the child appears to be a normal child of its age to-day. The striking thing in the case is that the disease ceased suddenly, and the child has been cured from the moment of the transfusion of the blood. . . ."

Comment.—Dr. Brewer's own words give the best comment on this remarkable case: "The latest accepted theories of melena neonatorum point not to ulceration or to gross lesions, but to the capillary blood-vessels as the seat of the bleeding, and the clinical picture of these cases is undoubtedly very like that of an infection as the etiological factor. But the course and the remarkable cure of the case reported here would seem

to disprove both the infectious theory of its origin and the blood-vessel explanation of the diapedesis of red cells and undisturbed osmosis resulting in the capillary hemorrhages. . . . At time of operation the baby was in a dying state and had palpably only a few hours to live—immediately after the baby was in perfect health. There was no period of convalescence. Such a sudden change in condition could not be due to a structural regeneration in the capillary vessels nor to a sudden overcoming of an infection; clinical experience will permit of no such inference. Neither the crisis of a pneumonia nor the relief of a spasmodic croup can be compared with the observed fact in this case, either from the point of view of reversal of pathological condition or of elapse of time necessary to bring it about. The only possible explanation of so rapid a change must be found in a chemical condition of the blood. And the final conclusion as to the nature of the disease is that melena neonatorum is a congenital malformation of the blood of unknown chemical nature. The solution of the problem of its etiology is to be found in a chemical study of the processes of osmosis in the capillary vessels, of the chemistry of the coagulation of the blood, and along kindred lines which are for the most part new and untouched."

CONCLUSIONS

Transfusion furnishes the ideal treatment for acute uncomplicated hemorrhages when the source of the hemorrhage can be reached and controlled. In chronic hemorrhages from the bowels of long duration transfusion will not only replace the lost blood, but may prevent further hemorrhage and effect a cure after all other measures have failed. If it does not bring about a permanent cure it usually gives a certain amount of relief. Certain cases of pathologic hemorrhage are cured.

CHAPTER XXVI

ILLUMINATING GAS POISONING

(*Group X*)

Up to the present time the author has had no personal experience with transfusion in clinical cases of poisoning from illuminating gas or charcoal fumes. When the high rate of mortality from these sources, and the largely unsatisfactory methods of treatment at our disposal are considered, it would seem to be entirely justifiable to use transfusion in cases which do not respond well to the ordinary means of treatment or which from the first are seen to be serious. Through the kindness of Drs. A. B. Kanavel and H. M. Richter the reports of 16 cases of gas poisoning from the various services of Cook County Hospital, Chicago, have been received by private communication. Statements based on the information furnished by these cases may render the matter more concrete, and emphasize the need of more efficient treatment than we now possess. The analysis of these cases is as follows:

Number of cases, 16.

Color of Skin.—Mentioned 14 times. Cherry red, 2; flushed, 1; cyanotic, 5; pale, 1; negative, 5.

Breathing.—Dyspnea, 15; apnea, 1 (this case was associated with morphin poisoning).

Coma, 15; mentally clear, 1.

Pupils reacted to light, 7 out of 11 times tested; 4 did not.

Musculature.—General tetaniform convulsions, 3; muscular tremor, 1; general rigidity, 2; stiff jaws, 2.

Pulse.—Variation 96 to 200 beats per minute. Eleven patients had as their highest pulse rate 120 to 160.

Reflexes (knee jerks).—Mentioned 12 times. Present 9 times; exaggerated, once; absent, twice.

Temperature.—Classified according to highest reached: 98° to 99° F., 1; 101° to 102° F., 1; 102° to 103° F., 3; 103° to 104° F., 1; 104° to 105° F., 1; 105° to 106° F., 2; 106° to 107° F., 3; 107° to 108° F., 2; 109.2° F., 1 case.

Treatment.—All received the usual stimulant drugs; 10 received oxygen inhalations; 4 were bled 10, 6, 4, and 8 ounces respectively; 5 received intravenous saline injections. All 16 cases died.

In general the treatment of gas poisoning has been along the following lines:

(*a*) Artificial Respiration. The indications for the use of artificial respiration are self-evident.

(*b*) Fresh Air.

(*c*) Oxygen. Oxygen is certainly indicated, not to oxidize the carbon monoxid, but gradually to displace it by being greatly in excess in the blood.

(*d*) Heat. Many persons have collapsed on being taken into the cold air, hence it would seem better to institute treatment in a warm room.

(*e*) Avoidance of Exertion. Patients have often died from exertion; for example, from violent endeavor to escape from a mine. There is probably acute dilatation of the heart in these cases.

(*f*) Stimulants. Camphor, caffein, digitalis, strychnin, etc.

(*g*) Venesection. This method is rational when combined with the injection of salt solution or blood. As to its use alone, it is condemned by most of the older writers on the ground that it further depletes a patient already in a low condition. On the other hand, Halstead reported 2 cases in which he

thought it did good. Halstead thought that no case had been saved by transfusion when venesection had failed. This was in 1884.

(*h*) Transfusion of Defibrinated Blood by the Older Methods, together with Venesection. This is mainly of historical interest. The theory was that venesection rid the body of some of the poison, and the transfusion replaced the lost hemoglobin with fresh hemoglobin. Löwenthal states that up to the year 1874 Landois had collected 15 cases of carbon-monoxid poisoning treated by transfusion. Of these the outcome was favorable in 6, unfavorable in 8, and doubtful in 1 case.

(*i*) Refusion of Blood. Halstead, in 1884, recorded a case treated by this method. The patient was comatose; respiration 28, shallow; pulse 96, small, easily compressible. There was general rigidity. Five hundred and twelve cubic centimeters of blood were withdrawn from the right radial artery, defibrinated, and strained. Two hundred and eighty-eight cubic centimeters were reinfused centripetally into the artery. The patient made a good recovery.

(*j*) Intravenous Saline Infusion. In the 80's the transfusion of blood was forsaken, and everyone turned to the new physiological saline solution. The following records have been found:

I. Jersey reported a patient in collapse for twenty-four hours. Was bled 8 ounces and given 11 ounces of salt solution intravenously. Patient recovered.

II. Wilkie reported 2 cases.

1. Bled 13 ounces; salt solution, 13 ounces; recovery.

2. Bled 6 ounces; salt solution, 13 ounces; death. Marked temporary improvement.

III. Schrüber reports a patient unconscious and in convulsions on the second day. Eleven and a half hours after having

been given saline infusion he began to speak and finally recovered.

IV. Von Gordon reports 3 cases:

1. Patient unconscious, slow stertorous breathing, pulse weak and irregular, 72 per minute, reflexes lost. Bled 300 c.c.; saline, 400 c.c.; recovered.

2. Patient unconscious, respiration irregular, pulse dicrotic, irregular, 120. Convulsions. Bled 300 c.c.; saline, 300 c.c.; recovered.

3. Patient unconscious, convulsions, dyspnea. Bled 165 c.c.; saline, 300 c.c.; recovered.

V, VI, VII, and VIII, from Cook County Hospital cases, all terminated fatally.

IX. Among other cases, Pilcher mentions 1 (Case II) in which venesection of 600 c.c. and infusion of 1,400 c.c. of normal saline solution when used with other remedies brought about recovery of a twenty-four-year-old male who was supposed to have been exposed to illuminating gas for about ten hours. At one time his temperature reached 106.8° F.

A few typical cases from the literature in which gas poisoning was treated by transfusion are as follows:

Case A. Stocker.

Gas Poisoning; Bleeding; Transfusion; Recovery.

The patient was a male, about fifty years of age, who was found unconscious in bed after exposure to carbon monoxid fumes. Stocker first saw him forty-two hours after he was found. He was then completely unconscious. He moved his limbs only slightly after strong irritation of the skin. He could not swallow and the bladder did not perform its functions. The respirations were 25 per minute and shallow. The pulse was full and regular, and beat 92 times per minute. After six hours the condition got worse, and as other means had failed to bring about improvement it was decided to transfuse. Before the transfusion 800 gms. of blood were removed. Then 110 gms. of defibrinated human blood were injected. Two hours after the transfusion the patient began to improve; he moved his limbs

a little, and first signs of returning consciousness appeared. Toward evening he could swallow, and later he began to talk a little. The urine was normal and remained so. The next day the pulse, respiration, and temperature were normal, and while from this time on convalescence was slow, it was uninterrupted. It took two months for complete recovery to follow. Stocker considered that the bleeding played an important part in the treatment, and that recovery was not due to the transfusion alone.

Case B. Löwenthal.

Illuminating Gas Poisoning in a Man Eighty Years of Age; Bleeding; Transfusion; Temporary Improvement; Death; Signs of Pneumonia Found at Autopsy.

Löwenthal's patient was a physician, eighty years of age, who was found unconscious in bed after exposure to fumes of illuminating gas. He did not respond when called or irritated. The pupils were reactionless. The pulse varied from 85 to 95 per minute. The blood-pressure was 135 mm. of mercury by a Basch sphygmomanometer. The respiration was spasmodic and stopped occasionally. Blood taken from the finger was dark cherry-red. The spectroscope showed the characteristic carbon monoxid spectrum. Stimulation of the phrenic nerve and artificial respiration were of no value in restoring consciousness. Camphor and ether injected subcutaneously, and also 200 gms. of normal saline solution, produced no effect. The patient was bled about 200 c.c., and then about 300 c.c. of defibrinated human blood were injected intravenously. Immediately after the transfusion the condition of the pulse was not essentially bettered. The soporific condition persisted. The respiration was stertorous, frequent, and superficial. In the next two days there was slight improvement, but death occurred on the third day after the transfusion without consciousness having returned. At the autopsy numerous purulent pneumonic foci were found in the left lung in the lower lobe, and also in the lower lobe of the right lung. The bronchial mucous membrane showed inflammation. There was softening of the inner lenticular nucleus of the brain.

Case C. Pilcher (Case I).

Illuminating Gas Poisoning; Bleeding; Saline Infusion with Temporary Improvement; Second Bleeding; Transfusion; Immediate Improvement; Recovery.

The patient was a woman, twenty-six years of age, who had gone to bed leaving the illuminating gas turned on. When found

the next morning she was comatose, her face was cyanotic, her lips purple, the pupils dilated, the extremities cold and cyanotic, and her temperature 100.4° F. The respirations were 80 per minute and stertorous. Small moist râles were heard in both lungs. At 10 A.M. 600 c.c. of dark venous blood were removed (it clotted very quickly), and 1,800 c.c. of normal saline solution were injected intravenously. The entire chest was cupped. Following the infusion the breathing became less labored, the pulse slower and stronger, and the cyanosis much less marked. At 3 P.M., however, the respirations became worse and of Cheyne-Stokes character. The general condition was not so good. Sixteen ounces of saline solution were given by rectum. The next morning the patient was still unconscious, the lungs showed beginning edema, and the temperature had risen to 103.6°. At 5 P.M. 300 c.c. more of venous blood were removed, and 480 c.c. of whole blood were transfused from the patient's husband to her veins by means of Aveling's apparatus. The immediate result was that the respirations became rapid, full, and stertorous, and the pulse stronger and fuller. The cyanosis faded somewhat. "The whole picture was as if a change for the better had taken place." Up to this time there had been no material change in the patient's condition except that the pulse showed good quality and the respirations had become less labored. A cold sponge bath was given, which was followed by marked improvement, and there was partial return to consciousness. The next day consolidation of the entire upper lobe of the left lung was found to have developed, but it soon cleared up, and from this time on convalescence was satisfactory. The patient was discharged three weeks after entering the hospital.

Case D. Hüter.

Carbon Monoxid Poisoning; Transfusion of Mixed Defibrinated Blood from Two Donors; Recovery.

A cavalry officer, twenty-six years of age, was found unconscious in his room owing to exposure to carbon monoxid fumes. Artificial respiration and stimulation of the phrenic nerves with electricity were employed, but the condition did not improve, and transfusion was decided on as offering the only chance the patient had for recovery. His respiration was very superficial and jerky, and intermitted every third or fourth time. The pupils did not react to light, and the corneal reflex was lost. The respiratory movements were the only spontaneous muscular movements which existed. A pound of blood

was removed from a medical student and from an orderly—half from each—defibrinated, strained, and almost all injected peripherally into the radial artery. At the same time the patient was bled about ½ pound. The blood was dark bluish-black in color. At the end of the transfusion the pulse was fuller, the beats stronger, and spontaneous respiration had returned. After half an hour the reaction of the pupils to light was apparent, and touching the cornea caused the eyelids to contract. The arm muscles moved a little, and later the patient had control of his tongue, and kept it from falling into the back of his mouth. At the same time the first vocal sounds were made, and consciousness began to return. For some days a soporific condition persisted. On the eleventh day the patient was discharged in good condition.

NOTE.—This case is of particular interest because blood from two different persons was mixed before being injected. There were apparently no gross evidences of hemolysis.

CASE E. SAMUELSON.

Carbon Monoxid Poisoning; Failure of Treatment; Transfusion; Recovery.

The patient was a man, fifty years of age, who was poisoned by fumes from burning charcoal. After all other methods of treatment proved to be ineffectual, transfusion of 4 ounces of defibrinated human blood was performed. Four hours after the transfusion there was still but slight change to be noticed, and the patient was put in a warm bath and had cold water poured over him. Three hours later the pulse and respiration were better, but the sensoria were still benumbed. Later on the sensoria returned and recovery was complete. Samuelson attributed the recovery to the transfusion.

CASE F. LÜHE.

Carbon Monoxid Poisoning; Small Bleeding; Transfusion; Injections of Spirits of Camphor; Recovery.

The patient was a man who was found unconscious from being exposed to carbon monoxid fumes from a stove. He was completely unconscious and his breathing stertorous. When taken to the military hospital his condition was as follows: He was in a completely reactionless coma with dilated and nonreacting pupils and a scarcely perceptible radial pulse, the rate of which could not be counted. The

apex beat of the heart could not be felt except that there was a weak trembling of the apical region. The face was slightly cyanotic, and the extremities cool. The respirations were 12 per minute, deep, and made with the help of the auxiliary respiratory muscles. There was also tracheal rattling, and the tongue was held behind clenched teeth. Before the transfusion from 40 to 50 c.c. of dark cherry-red blood were withdrawn with difficulty. Then defibrinated human blood was injected into the radial artery (amount "scarcely 100 c.c."). This was followed by subcutaneous injections of spirits of camphor. A half hour after the transfusion the first signs of reaction were shown by muscular movements and weak reaction of the pupils. Later the temperature rose slowly. By that evening consciousness had returned so that the patient could answer questions by "Yes" or "No." The next morning there were signs of a beginning pneumonia, which cleared up under treatment. Later convalescence was once more interrupted, but recovery finally followed. On the fourth day after the transfusion the urine was darkly stained, but whether by the increase of the normal urinary constituents or by the presence of blood pigments was not determined.

Case G. Uterhart.

Carbon Monoxid Poisoning; Bleeding; Transfusion; Rapid Recovery.

The patient was a male, sixty-five years of age, who was found apparently dead in his home after inhaling carbonic oxid gas. A physician brought back the almost extinct respiration by irritating the phrenic nerve, and the patient was then brought to the hospital. He was there found to be very much run down and emaciated, was covered with eczema from scabies, and had a bedsore on the left trochanter the size of a thaler. He did not react to calling, touching the skin, oı pinching. The respirations were regular, but at the rate of 14 per minute and shallow. There were loud tracheal rattlings. The pulse varied between 60 and 70 beats per minute, and was easily compressible. Percussion of the lungs showed nothing abnormal. Râles were heard in the left lung. The patient was bled a few ounces, and then about 10 ounces (probably) of defibrinated human blood were injected into his median basilic vein. Improvement began to be shown almost immediately, partial consciousness soon returned, and he was able to drink coffee. The respiration was deep, the pulse more frequent and stronger. That night he slept well, and recovery was interrupted and rapid.

Case H. Riedinger.

Illuminating Gas Poisoning; Transfusion of at Least One Half Liter; Death.

The patient was a woman, thirty-nine years of age, who was removed from her bedroom in an unconscious condition from exposure to escaping illuminating gas. When brought to the hospital she was unconscious, the eyelids were closed, the pupils were without reaction, bloody foam was escaping from the mouth, and the jaws were locked. The respiration was very labored and stertorous. No dullness was found over the lungs or heart. The pulse could not be felt. The temperature was 36.5° C. The cold extremities did not react to irritation. The patient was given a rectal injection of cold water, mustard was applied to the chest, and ergot injected. After nine hours had elapsed she was in the death-agony, and then at least ½ liter of defibrinated human blood was injected into the median vein. The immediate result of the transfusion was an improvement in the breathing, the trismus disappeared, and the next morning the temperature was 39.2° C., the pulse 126, and the breathing 44 per minute. In spite of this there was rapid failure, and death occurred in the evening.

Autopsy.—The principal points of interest were as follows:

The dura mater contained abundant fluid and the spinal cord was hyperemic and edematous. The posterior portion of the lenticular nucleus was hyperemic in spots. In the right heart there was a large amount of semi-fluid light-brown blood. The left heart was absolutely empty. There were some pericardial ecchymoses. The left lung was moderately adherent, but pervious throughout. The lower lobe was apparently larger than the upper, bluish-red and hyperemic, with nowhere firm consolidation. The right lung was apparently heavier than the left and very edematous. In places there was a beginning firm infiltration. No clots were found in the pulmonary vessels. The spleen was very soft and injected with blood. The liver was apparently unaltered. The kidneys were hyperemic in places.

Case I. Garrigues.

Illuminating Gas Poisoning; Bleeding; Transfusion from a Negro; Recovery.

The patient was a male, forty-two years of age, of excellent constitution, who blew out the gas just before retiring for the night.

His room was the size of the ordinary hall bedroom, and there was one burner from which the gas escaped. The next morning he was found unconscious. Hot bottles and mustard plasters were applied to the skin, the feet were rubbed with a stiff brush, and artificial respiration was begun. When Garrigues saw him at 8 A.M. his face was pale, the conjunctivæ injected, the pupils completely dilated and immovable. There was a well-marked strabismus internus. The respiration was puffing and at the rate of 22 per minute. The radial pulse was barely perceptible and 108 per minute. Reflex action was active, but consciousness was completely gone. The patient frequently ground his teeth. Some subsultus tendinorum was observed, and all the muscles were in a high state of contraction, especially the flexors. The hands were clenched, the arms bent over the chest, and the knees drawn up.

The patient was at once bled from a branch of the basilic vein until the radial pulse of the other side became very small (the exact amount removed was not stated). Then about 6 ounces of defibrinated blood from "a strong and healthy young negro" were injected into the same vein. This was done so slowly that it took about three quarters of an hour. During this time the pulse fell to 92 per minute, and the breathing "became so natural in character as to resemble that during normal sleep," although the same rate was maintained. When the transfusion was finished the patient could be sufficiently roused to swallow some ammoniated water and some black coffee, but as he was still very sleepy, he was constantly roused by flagellation and the application of a faradic current. At 7.30 that evening the patient laughed and chatted cheerfully and had only a slight headache. Further recovery was uneventful.

NOTE.—This is the only instance which has been found of transfusion from the colored to the white race.

CASE J. VLEMINCKZ.

Carbon Monoxid Poisoning; Bleeding; Transfusion; Recovery.

The patient was a coachman who was poisoned by vapor from a charcoal stove (brazier). He retired at about eleven at night and was found unconscious the next morning. He had vomited a great deal, and was rattling in his throat. When received at the hospital he was in a state of profound collapse with complete abolition of all his senses, and his intelligence. His face was livid with a violet hue, the lips were bluish, and the superficial veins of the neck

swollen. The eyes were closed, the conjunctivæ injected, and the pupils widely dilated. The respiration was jerky, "anxious," and accompanied with numerous râles which could be heard at a distance. A brownish foam escaped from the mouth. The heart beats could not be heard and the pulse was almost imperceptible. The skin was warm except at the extremities, where it was like ice and cyanotic. Sensibility was deadened, but not abolished. After trying different remedial measures, there was no amelioration of the condition, and convulsions appeared, the temperature steadily fell, as the patient became worse. It was then decided to transfuse, and leeches were applied and the patient bled. The blood was of blackish appearance and clotted very rapidly. About 150 gms. were removed. At this time the patient seemed to be more deeply comatose, and the tetanic convulsions came almost without interruption. At times the heart ceased to beat, the respirations slowed and were very irregular. The corneal reflex was abolished and the pupils widely dilated.

Defibrinated human blood was used, and 67 gms. were injected into one of the branches of the internal saphenous vein in twenty minutes. During the operation no change was perceptible. Immediately after, the heart seemed to beat with more force and the pulse was better. Soon there was a violent chill, the pulse occasionally was almost imperceptible, and the convulsions stopped. The chill lasted forty-five minutes. After this, recovery of consciousness and sensibility was slow but steady, and the patient made a slow but uneventful recovery. Spectroscopic examinations of the blood showed the presence of carbon monoxid.

Vleminckz emphasizes the following: "That a relatively small quantity of normal blood (67 gms.) was sufficient to rapidly dissipate the most grave toxic phenomena. Evidently all the blood mass was not disintoxicated, since, eight days after the transfusion, the spectral analysis still showed the existence of feeble traces of oxid of carbon, but it was enough to cause the reawakening of the functions of the organism and return life to a dying person. . . ."

CONCLUSIONS

While the author, as previously stated, has had no personal experience in transfusing for illuminating gas poisoning in human beings, he feels that the experiments on dogs and

the cases reported by other observers show that it may be a life-saving measure. As indicated in the preceding pages, it should be preceded by free bleeding. In severe cases it would seem to be justifiable to resort to bleeding and transfusion before trying other measures.

CHAPTER XXVII

MISCELLANEOUS CASES

(*Group XI*)

CASE NO. XI, 1 (6,855). ABSTRACT. CONSULTATION WITH DR. J. W. LEHR, WOOSTER, OHIO.

Adenocarcinoma of Uterus; Panhysterectomy; Suppression of Urine; Anuria for Twelve Hours; Failure of Response to Treatment; Transfusion; Death Twelve Hours Later without Change in Symptoms.

The patient was an American woman, fifty-four years of age, with negative family history. She had had the usual diseases of childhood and pneumonia three times, the last attack coming five years previously. The menopause occurred when she was forty-seven years old, and was normal. She had five children, and had had two miscarriages twenty-five years previously.

Eight months previously she had had bleeding from the vagina, the blood coming away with a rush. Since then she had had several hemorrhages, and slight bleeding at intervals. Four months previously a serous, nonirritating discharge began. She was constipated, and lost five pounds in weight.

The physical examination showed the patient to be fairly well nourished, but of a pasty, flabby type, with weak heart action and hair prematurely gray. Her uterus was enlarged and tender. The cervix was hard and nodular, and there was a foul-smelling hemorrhagic discharge. The diagnosis of carcinoma was made.

At the operation a panhysterectomy was performed by the abdominal route under ether anesthesia. There was marked venous hemorrhage, and the patient, who was in an exaggerated Trendelenburg position, showed symptoms of acute cardiac dilatation. The position was immediately changed to one more nearly horizontal, and the venous hemorrhage allowed to proceed rather freely in order to relieve the heart. Otherwise the operation was without incident. The pathologist reported the tumor to be an adenocarcinoma.

After the operation the secretion of urine first became scanty and then stopped altogether. The patient suffered no pain and seemed to be entirely comfortable. The heart action was weak and the blood-pressure very low. In spite of a full dose of digitalis and strychnin the heart was incapable of performing the necessary amount of work and the kidneys would not secrete. In twelve hours there was no response to infusions of normal saline solution, counter-irritation over the kidneys, or the other measures which were employed. As a last resort, and with but little hope of success held out to the relatives, transfusion was proposed.

A daughter of the patient served as donor. One of her radial arteries was anastomosed to a venous branch of the patient near the elbow by the cannula method. The blood was allowed to flow across for twenty-four minutes.

As the patient presented only an occasional pulse beat at the wrist, her blood-pressure could not be taken with accuracy before the transfusion. At the end of the transfusion the pressure had risen to 76 mm. of mercury. The pulse rate fell from 168 to 154 per minute. The red count rose from 3,488,000 to 3,680,000, the hemoglobin did not show any change, and the white count fell from 56,000 to 46,600. The renal complication, however, was not overcome, and death occurred twelve hours later.

Comment.—The condition to be overcome in this case was entirely apart from either hemorrhage or shock, and there was very little hope of any material benefit. The transfusion, as stated above, was undertaken in despair of other treatment. Clinical and experimental observations have led to the view that transfusion will not prove to be of value in this type of case.

The statistics of the donor are as follows:

The Donor

Time	Red Count	Hemoglobin	White Count
Before transfusion	5,148,000	100%	6,000
After transfusion	5,120,000	100%	9,040
Seven hours after	4,800,000	90%	8,000
1st day	4,820,000	90%	8,400

(See Chart, Fig. 25, p. 122.)

Case No. XI, 2 (7,369). Abstract. Consultation with Dr. T. W. Ranson.

Puerperal Eclampsia; Patient brought to Hospital in Unconscious Condition; Immediate Cæsarean Section; Delivery of Living Child; Transfusion for Thirty-five Minutes with Simultaneous Bleeding of 140 c.c.; Hot Packs, Constant Rectal Irrigation, etc.; Uninterrupted Recovery.

The patient was an American woman, twenty-three years of age, who had convulsions. One of her sisters died of "dropsy." Otherwise her family history was negative. She had had a mild attack of typhoid fever two years previously.

The patient was a primipara. She expected to be confined about two weeks after the time when she was brought to the hospital. For a month previously she had had marked swelling of her lower limbs and frequency of micturition. For two weeks previously she had had puffiness of her face in the morning, particularly about her eyelids. The evening before entrance she complained of headache, but ate a good supper and seemed to be cheerful. She slept well up to midnight, and then was restless until morning. On getting up at 7.30 A.M. she suddenly said she could not see, began to mumble unintelligibly, and vomited. She was put back to bed and at once had a convulsion, her body becoming stiff, froth coming out of her mouth, and her eyes beginning to stare. She became blue in the face and trembled somewhat, but not violently. During the rest of the morning she was in this condition much of the time. When Dr. Ranson was called in he ordered her to be taken to the hospital at once. On the way she had two convulsions in the ambulance.

A careful physical examination could not be made, owing to the urgency of the case. The patient was unconscious. She threw herself about on the bed. Her face was markedly edematous, especially about the eyes. Her skin had a nephritic pallor. There was considerable edema of the limbs. The heart sounds were clear. There was slight cardiac hypertrophy.

The patient was immediately etherized. The pregnant uterus was exposed by a median incision, incised, and the baby removed. The baby at once gave a lusty cry, and from then on showed nothing abnormal. The placenta was removed, the uterus sutured, and the abdomen closed in the usual way. The hemorrhage was not marked.

A radial artery of the patient's husband was hastily connected with a median basilic vein of the patient by the cannula method.

The blood was allowed to flow across for thirty-five minutes. As it flowed the patient was bled 140 c.c. and was kept under light anesthesia.

After the transfusion the patient was taken to the ward. Hot packs were given for twenty minutes every four hours. A magnesium, glycerin, and water enema was given, and 2 gms. of aseptic ergot subcutaneously. There was some bleeding *per vaginam*. Constant slow rectal irrigation was also given. During the night consciousness returned. The bowels moved freely, the kidneys were active, and she perspired freely. A milk diet was ordered.

The day after the transfusion there was much less edema of the face. That of the limbs had disappeared. The patient was told of the birth of the baby, and seemed much surprised, as she had no recollection of what had happened since she had her first convulsion. She knew nothing of the laparotomy. She voided freely. The urine was becoming normal. Nineteen days after the laparotomy she had a caked breast. Twenty-one days after she was discharged. Except for the caked breast the convalescence was uninterrupted. The child remained well.

It should be stated that before the transfusion, hastily made hemolysis tests showed no autolysis, or hemolysis of the donor's corpuscles by the patient's serum. Reverse hemolysis occurred, however—i. e., the serum of the donor hemolyzed the corpuscles of the patient.

Comment.—Just what part the transfusion played in this case can not at present be determined. Similar cases recover after the uterus is emptied, and therapeutic measures such as those used are employed. In severe cases immediate Cæsarean section under nitrous oxid, followed by bleeding and transfusion, may prove a valuable method, provided, of course, the patient has not already received mortal visceral lesions.

SUMMARY

Case No. XI, 1 (6,855).

Transfused.—For acute suppression of urine following panhysterectomy for adenocarcinoma of uterus.

Immediate Result.—Inconsequential.

Other Treatment.—Digitalis, strychnin, saline infusions, counterirritation over kidneys (all before the transfusion).

Late Result.—Death twelve hours after transfusion.

Case No. XI, 2 (7,369).

Transfused.—For puerperal eclampsia with convulsions and coma.

Immediate Result.—Beginning improvement.

Other Treatment.—Before the transfusion, Cæsarean section (birth of living child). During the transfusion, patient bled 140 c.c. After the transfusion, hot packs, constant rectal irrigation.

Late Result.—Uninterrupted recovery of mother. Child remained well.

MISCELLANEOUS CASES FROM OTHER SOURCES

Case A. Lange.

Puerperal Convulsions in a Secundipara; Delivery of Dead Child; Application of Different Remedies without Result; Patient Bled 14 Ounces and Transfused 7 Ounces; Thirty-third and Final Convulsion a Half Hour Later; Uninterrupted Recovery.

The patient was a young woman, twenty-three years of age, who had had a child two years previously without abnormal conditions arising. On examination edema of the under eyelids was found as well as of the lower extremities. Convulsions with subsequent coma occurred about two weeks before the expected time of delivery. The urine contained a large amount of albumin. The cervix was dilated by means of a colpeurynter, and a dead child was delivered. Termination of the third stage of labor was followed by the uterus contracting well. Then more convulsions occurred which were as severe as the previous ones. Twelve leeches were applied to the patient's head, and also ice. Enemata were given, morphin was injected hypodermically, chloroform was inhaled by the patient, and cold "irrigations" of the head were given—all without

result. Up to that time 32 convulsions had occurred. The patient lay in deep coma with stertorous, rattling breathing.

As soon as it was decided to transfuse, the patient was bled 14 ounces. About 7 ounces of defibrinated human blood were then injected intravenously. Immediately after the transfusion the pulse was smaller and more frequent and the cyanosis of the face began to diminish. After half an hour the thirty-third and last convulsion occurred. It was less severe than the others had been. Soon after the patient began to sweat all over. At end of another hour the breathing was no longer stertorous, and the first signs of consciousness appeared. A little later she fell asleep and slept all night. Two days after the transfusion she was entirely conscious. An uninterrupted convalescence followed.

Case B. Watts.

Extensive Superficial Burn; Transfusion; Recovery.

"The child, three and a half years old, was admitted on February 20, 1907, with an extensive superficial burn, involving the right half of the trunk, right arm, right side of face, and, to a slight extent, the left arm and right leg. After being admitted to the hospital the condition of the patient became rapidly worse, and in forty-eight hours it was critical; the pulse which, on admission, was 128 to the minute, was then 180, but of fair quality; the temperature which, on admission, was 99°, had risen to 105°. The child was quite dull and hard to rouse. The following day the temperature was 103.8° and the pulse 170 to the minute, but its quality was poorer than on the previous day and the stupor was more pronounced, it being very difficult to rouse the child to take nourishment. In view of the toxic condition, high temperature, and rapid pulse, it was decided to do a direct transfusion of blood, a relative of the patient consenting to give the blood. The operation was done practically as in the foregoing case, except that on account of the small size of the donee, the brachial vein was used instead of the basilica. The suture was quite satisfactory, considering the small size of the vessels. On turning on the blood stream the vein became considerably distended and pulsated actively, and it seemed as though the child was receiving a considerable amount of blood. Blood-pressure observations on the child, however, showed no increase in pressure during the thirty to forty minutes during which the transfusion continued. After this time pulsation in the vein ceased, and it was thought that thrombosis had occurred; accordingly,

the vessels were ligated, and that portion containing the suture was removed for examination. This examination revealed a small thrombus, adherent to the line of suture, which had probably occluded the vessel. The donor was little, if at all, affected by the bleeding. As said above, there was no increase in the blood-pressure of the donee, so it was not considered wise to bleed from the opposite arm. Although it may be a case of *post hoc ergo propter hoc*, the child improved rapidly after the transfusion, and is now (March 20, 1907), apparently on the road to recovery, though the temperature continues somewhat elevated."

CASE C. COLE.[1]

Pellagra; Transfusion from a Donor who had Previously Recovered from Pellagra; Marked Improvement; Recovery.

The patient was a negress, thirty-five years of age, whose symptoms of pellagra had developed three weeks previously. She had progressed downward rapidly, with marked loss of weight and strength. At the time of the transfusion she was unable to move her hands or head from extreme asthenia; in fact, even deglutition and phonation were basely possible. There were no distinct blood changes other than those of a secondary anemia. The donor was a healthy negress, thirty-six years of age, who had recovered from a severe attack of pellagra in the fall of 1907. Transfusion was performed by the cannula method, the blood flowing over in a good stream for twenty minutes. Then, as the donor showed signs of syncope, the flow was stopped, and the wounds were sutured. Both women left the tables in good condition. Twenty-four hours after the transfusion, August 4, 1908, the patient showed marked mental and general improvement. Three days later the improvement had continued. There was marked desquamation of the skin lesions. One week after the transfusion the patient was able to walk around the yard. There was marked gain in weight. Progress to a perfect recovery was rapid. At the present time, four months after the transfusion, the patient is in as good health as she was in before the attack of pellagra occurred. In regard to this case Dr. Cole says: "We draw no definite conclusions from the recovery in this case, but we believe the coincidence to be very suggestive, especially considering the condition of the patient and the high mortality rate—64 per cent in the cases reported by Searcy."

---

[1] From a private communication from Dr. H. P. Cole, now of Mobile, Ala.

CASE D. WATTS.

Extensive Burn; Transfusion; Death.

"This patient, four years old, was admitted to the hospital with an extensive burn, involving the greater portion of the trunk, the face, the thighs, and parts of the arms. Her condition was critical, and in spite of appropriate treatment steadily became worse, until, twelve hours after her admission, it was such that it was decided to do a transfusion of blood, intending, if possible, to raise the blood-pressure to such an extent that the child might be bled from the opposite arm. At this time the child was pale, its extremities were cold and clammy, it was vomiting frequently, and its pulse could hardly be felt. A man in one of the public wards kindly consented to give the blood, and the operation was done exactly as in the preceding case (i. e., by arteriovenous anastomosis). The anastomosis was very satisfactory. On removing the clamps the vein became distended and pulsated actively, and when pressure was made upon the vein it became so distended in the region of one of its valves that it looked as though it would burst. The transfusion was continued for eighty-three minutes, when the vein was divided and the blood found to be running at the rate of 4 c.c. to the minute. It was thus estimated that the donee had received 332 c.c. of blood. That portion of the vessels containing the suture was removed. On being opened it was found to be perfectly smooth and no thrombus was present. The condition of the child improved somewhat during the transfusion, its color improved, and the quality of the pulse became such that it could be counted. The improvement was, however, disappointing, and far from enough to warrant bleeding from the opposite arm. The donor showed the effects of the bleeding very little, his blood-pressure falling from 120 to 105. The improvement of the child was of short duration, and it died about six hours after the transfusion was completed."

CHAPTER XXVIII

GENERAL RECAPITULATION OF TRANSFUSION

The transference of whole or modified blood, by various methods for numerous purposes, from an individual of the same or of alien species to another, has been practiced in many parts of the world for at least four centuries. A critical historical review of this work with reference to the results accomplished may be summarized as follows:

The greater part of it was done crudely and empirically before the development of chemistry, physiology, pathology, and bacteriology, and before the period of good hospitals and surgical instruments. There were many accidents arising from infection, clotting, the use of alien blood, and unfortunate selection of cases, so that with the advent of normal saline solution as a substitute for blood, transfusion of blood was no longer practiced.

From clinical and experimental research into the technic of transfusion it is concluded that the vascular systems of two individuals may be united so that intima comes in contact with intima only; that this may be best accomplished by a special anastomosis tube, also by the Carrel suture; that blood may be transferred without clotting; that the use of the radial artery of the donor and any superficial vein of the recipient yields the best results; that the operation may be done painlessly; that the blood lost by the donor is regained in from four to five days; that the amount transferred is under the immediate control of the operator, and that the rate of trans-

ference should be gauged carefully and kept within the limits of physiologic safety.

EXPERIMENTAL

The effect on the blood and tissues in transfusion between two normal animals of the same species was first investigated. Normal dogs were bled to the limits of safety and an equal amount of blood transfused from other normal dogs. Later the experiments were reversed, the blood from the recipient being transferred to the first donor. A third animal was then used as a donor and the same experiment performed. After a similar period this was reversed. On repeating the bleeding and transfusion, retransfusion, and a second transfusion, and then introducing the blood of a third animal, no ill effect was noted. The dogs remained in normal health. The transfusion of a number of animals without previous bleeding proved likewise harmless. Complete metabolism observations by Professor Haskins, of Western Reserve, and Professor Folin, of Yale, did not show important changes. Likewise, a complete metabolism determination in a clinical case was negative. Many microscopical observations of the blood-picture of the recipients were negative as to any abnormal changes. No hemoglobin was found in the urine. It was, therefore, concluded that the blood of one normal dog is physiologically interchangeable with that of another of the same species.

The effect of an *overtransfusion*, utilizing very large dogs as donors and small ones as recipients, was next investigated. As a result it was found that if transferred rapidly, that is, with a full head stream from the carotid artery of the donor into the jugular vein of the recipient, edema of the lungs in some instances followed. On the other hand, when the overtransfusion was done more slowly, so as not to embarrass the right heart and the pulmonary circulation, a huge donor and

diminutive recipient being utilized, the blood was successfully transfused, the abdomen in time became enlarged and gradually increased in size until it became so tense that the diaphragm and the movable ribs were immobilized and the animal died of asphyxia. The autopsy findings proved that both the liver and the spleen may be ruptured by excessive transfusion.

Transfusion in the normal animal caused an immediate rise in the blood-pressure. This rise in some instances continued until it had doubled the normal. After the maximum had been reached there was usually a decline, though the pressure as a rule remained higher than normal. These results were materially different from the results of intravenous infusion of normal saline solution. The infusion of normal saline solution raised the pressure of a normal animal slightly, if at all, even when infused from a high column through a large tube under a strong head of pressure. Whereas normal salt solution will not sustain the pressure at a higher level than normal, direct transfusion of blood may, and usually does so. It was found that at death an overtransfused animal might show a residual pressure of from 15 to 30 mm. of mercury. It was also found that animals recently killed, then subjected to transfusion, might show a rise in carotid pressure as high as 60 mm. of mercury. The latter contrasts with the rise under parallel conditions of 10 to 15 mm. mercury by saline infusion. Blood transfusion exerts a greater influence on the blood-pressure than does saline infusion.

After having found that blood of normal animals of the same species is physiologically interchangeable; that the blood-pressure in the normal animal may be raised and sustained; that if the transfusion be given with too great rapidity the pulmonary circulation may be so embarrassed as to produce an acute and even fatal edema of the lungs; that if the trans-

fusion is given more slowly the blood may be transferred from the pulmonary to the systemic circulation with safety; that an excessive transfusion thus given may cause serious damage to the abdominal viscera, even causing immediate death; and after having established a safe technic and the limits of safety, attention was turned to some of the problems that might have a clinical bearing. The first was hemorrhage.

Hemorrhage.—Every degree of hemorrhage was treated, even after the cessation of respiration and of the heart beat. A separate group of experiments was made as a means of comparing the value of direct transfusion with other methods. In every instance, after complete failure of current methods, including maximum saline infusion, so long as there was even an auricular beat, the animal could be resuscitated by direct transfusion.

On investigating the effect of excessive bleeding followed by transfusion, in the treatment of strychnin poisoning, it was found that strychnin probably formed a loose chemical combination with the fixed tissues of the body, and did not, therefore, yield to treatment.

In order to test the value of bleeding in certain types of toxemia, a number of observations were made with diphtheria toxin. It was found that the animals that were bled, then transfused at the onset of the symptoms, usually occurring about twenty hours after the injection of the diphtheria toxin, were no more likely to recover than the control animals. Then on gradually reducing the time to sixteen, twelve, eight, four, and two hours, it was found that the animals, even in these periods, before any symptoms of toxemia appeared, were not favorably influenced, although an animal bled and transfused within one-half hour after a fatal dose showed some benefit. It was evident that here, too, chemical combination with the fixed tissues of the body occurred, and that this fixa-

tion when once made was not affected by bleeding and transfusion.

Another series of experiments was made, consisting of performing bilateral nephrectomy on dogs, and then testing the value of repeated bleeding and transfusion in the resulting condition. Life was but little prolonged and the results were virtually negative.

Illuminating gas poisoning is produced because carbon monoxid has a greater chemical affinity for hemoglobin than oxygen; therefore, when a sufficient amount of gas comes in contact with the inspired air, the hemoglobin is saturated with carbon dioxid, and oxygen cannot be carried by the red corpuscles. The tissues must, then, depend on the supply of oxygen in solution in the blood plasma. This, under partial pressure of oxygen in atmospheric air, is insufficient to sustain life. The opinion of Halstead and other observers as to the value of transfusion after bleeding was verified. So long as there was any circulation the animal could readily be resuscitated. No later ill effects were noted. This method was contrasted with inhalation of oxygen under pressure, with forced respiration, and with the administration of saline infusion, and was found to yield the best results.

Surgical Shock.—Surgical shock is a term designed to cover a group of phenomena due to certain altered physiologic functions. The essential characteristic from the view-point of the practical surgeon is the state of lowered blood-pressure. So long as the pulse is satisfactory the surgeon entertains no fears for the safety of the patient. So far as is known, death from shock is due to failure of the circulation—a failure to supply the brain with sufficient blood—an intravascular hemorrhage. So far as present evidence goes, the chief cause of the failure of the circulation is a functional breakdown of the vasomotor nerve mechanism. Once the pressure is low the

disabled centers suffer still more. In a restricted sense, there arises a species of vicious circle; viz., the blood-pressure is low because of the failure of the vasomotor nerve mechanism, and because of the consequent anemia this disabled mechanism is not able to do as much work as under a normal blood supply. To overcome the anemia of this and other tissue should be the therapeutic object. With these facts in mind it was sought to ascertain whether or not by the transfusion of blood the inefficient blood volume might or might not be sufficiently increased to fill up the relaxed vascular system, to cause more blood to reach the heart, and so to increase the outflowing stream, and, hence, help to overcome the anemia, which in turn would be followed by an increased activity of the vital centers, thus supplanting the vicious circle of anemia by the beneficent circle of hyperemia.

It was shown experimentally that in every grade of shock transfusion produced a rise in the blood-pressure, frequently to the normal, occasionally above it, and sustained it well.

After the striking effects of transfusion in the treatment of shock were fully established, another series of experiments was undertaken to determine what, if any, effect a careful overtransfusion in a normal animal might have in the prevention of shock. It was found that animals carefully overtransfused (so as not to embarrass the pulmonary circulation, on the one hand, or overcharge the abdominal viscera, on the other), and then subjected to shock-producing procedures, could not be *immediately* killed by shock alone. The blood-pressure could be reduced to a certain degree, lower than which it was not possible to reduce it by trauma alone.

On extending the experiments it was found that in such overtransfusion traumatizing the spinal cord produced either a rise or no material effect. The medulla was then destroyed, after which, by maintaining artificial respiration, the

circulation was not impaired. Finally, the supreme test was made of decapitating such overtransfused animals, and it was found that the blood-pressure was still evenly sustained without other assistance than artificial respiration. Even when respirations were not given, the height of the pressure was not changed until affected by asphyxia. One such overtransfused decapitated animal "lived" over three hours by merely maintaining artificial respiration. This remarkable circulatory state is readily understood by considering for a moment one phase of the physiology of the heart beat. Even when the heart has been removed and kept on ice for a day or more, if oxygenated defibrinated blood under pressure of from 80 to 100 mm. mercury be circulated through the coronary vessels it may beat again and continue beating for a number of hours. As Sollman has shown, even a coronary pressure raised to that height by metallic mercury may cause the inauguration of the heart beat. In the overtransfused animal the vascular system may be so filled with blood that its elasticity is utilized to create a resistance against which the heart may act, resulting in a pressure of from 80 to 140 mm. of mercury in the aorta, and hence in the coronary artery. There is no reason, therefore, why the heart should stop beating so long as the elasticity of the vessels gives the necessary peripheral resistance for the maintenance of the coronary pressure, hence bloodless decapitation in this state causes no immediate fall in the blood-pressure.

Sarcoma.—In 10 cases of transplantable lymphosarcomata in dogs bleeding and transfusion from donors immune to lymphosarcoma was followed by complete regression of the tumors in 7 cases; in 2 of the remaining ones there was a very marked effect from the transfusion, while one dog died without showing any tumor regression.

CLINICAL

Hemolysis.—While hemolysis occurs rarely, if at all, in the normal state, it does occur in certain diseases. When there is time hemolysis observations are made on the blood of the proposed donor and the recipient. This test requires at least twenty-four hours. By making the hemolysis test of the proposed donor and of the recipient harmful blood reactions may be obviated, though the reactions *in vitro* are not the same as *in vivo*. In the opinion of the author, agglutination may be disregarded.

In every instance in 73 clinical cases the technic of both cannula and suture anastomoses was successfully performed.

Pernicious Anemia.—In one case of extreme pernicious anemia transfusion was followed by temporary improvement, but almost immediately subsequent to the transfusion there was a rapid hemolysis of the blood transferred. There was no evidence that the course of the disease was modified.

Leukemia.—A patient with myelogenous leukemia that had resisted careful medical treatment, including X-ray treatment, was first bled, then transfused. Though there was a marked temporary gain in vitality, as manifested by an improved well-being and increased appetite and strength, the blood picture showed no change. There was no evidence that the natural course of the disease was modified.

Sarcoma.—Transfusion after excision of sarcoma gave some apparent encouragement, though the benefits are extremely doubtful. Transfusion in the inoperable cases cured none.

Carcinoma.—Transfusion showed no influence on carcinoma.

Hyperthyroidism.—Neither transfusion nor bleeding with transfusion relieved the symptoms of hyperthyroidism. There

is probably a chemical combination in the fixed tissue of the body.

In **tuberculous peritonitis** there was immediate improvement in the general condition of the patients following the transfusion. Very weak persons were transformed into safe surgical risks, permitting safe excision of tuberculous adnexæ. The unusually favorable subsequent course in this group of cases suggests the possibility of special therapeutic value.[1]

Chronic Suppuration.—For the double purpose of lessening the secondary anemia and possibly supplying normally active leucocytes in extreme cases of prolonged intractable suppuration, transfusion was done. There was distinct improvement in the vitality and general well-being. In some instances the improved blood picture did not continue, neither was there any noticeable improvement in the local suppurative field. Some of the patients, however, gained markedly in weight and in strength, and in every case it was demonstrated that the patient could be raised to a higher state of vitality for the better endurance of surgical measures.

Shock.—Bad surgical risks have been rendered safe by a preliminary transfusion, or by transfusion during operation. On experimental grounds normal subjects who are to submit to operations involving great surgical shock may be rendered at least partially immune to shock by a preliminary transfusion. The timely treatment of uncomplicated surgical shock by transfusion has been effective. In some cases it seemed to act as a specific cure.

Acute Hemorrhage.—In uncomplicated hemorrhage, when treated *before the central nervous system has become irreparably damaged by anemia,* transfusion is a specific remedy.

[1] The results of later work on pulmonary tuberculosis are more encouraging.

In **typhoid hemorrhages** the patients were remarkably revived, but the hemorrhages recurred. The patients were transformed from a dying state to a surgical risk apparently sufficiently good to endure laparotomy. In grave cases the advisability of attempting to secure the bleeding vessels should be seriously considered.

Chronic Hemorrhage from the Bowels.—In five cases of chronic hemorrhage from the bowels, extending over a period of from one to five years, and having resisted medical treatment, transfusion was done. Four of these cases were relieved by a single transfusion, in one slight hemorrhages have recurred, but the remaining four are well. In one instance there was only temporary improvement following the first transfusion, but the second transfusion gave relief.

Hemophilia.—In one case of fairly well-marked hemophilia an intractable nasal hemorrhage was immediately arrested by direct transfusion.[1]

Purpura.—In one case of purpuric hemorrhage transfusion was followed by relief; in another relief was only temporary.

Pathologic Hemorrhage Accompanying Jaundice.—In one case the hemorrhage was immediately arrested by transfusion, in another hemorrhage recurred.

CONCLUSIONS

Transfusion, when properly safeguarded, may be safely done. In pernicious anemia, toxemia, certain drug poisonings, leukemia, acute hyperthyroidism, carcinoma, and uremia it has been of no value. In tuberculosis and chronic infec-

[1] Two very recent cases of hemophiliac bleeding have shown immediate response to transfusion, but the bleeding recurred soon to be followed by hemostasis again, and general improvement. As yet a final conclusion as to the permanent benefit is hereby warranted. There is no doubt as to the immediate benefit.

tions it has certain value. Transfusion of blood from an immune animal has cured sarcoma in dogs. In human sarcoma there is some evidence of value, though it is not yet proved. In pathologic hemorrhage it is of marked value. If done in time, transfusion is specific in acute hemorrhage. In suitable cases it seems to be almost specific in the prevention and treatment of shock.

Judiciously employed, transfusion will surely prove a valuable, often life-saving, resource; injudiciously employed, it will surely become discredited.

BIBLIOGRAPHY

BIBLIOGRAPHY

Chapter III

1. Moulin, A. The Quantity of Blood in Man and the Celerity of its Circulation. Phil. Trans., Lond., 1700, III, 225. Quoted from Flint, A., Human Physiology, 1901 ed.
2. Hoffman. See Flint, A., Human Physiology, 1901 ed.
3. Lehman and Weber. *Ibid.*
4. Hayem, G. Du sang. Paris, 1889, 207.
5. Dastre, A. Sur le degré de confiance que méritent les déterminations de la quantité totale du sang. Arch. d. physiol. norm. et path., 1893, 5s., V, 787.
6. Stewart. A Manual of Physiology, 1900 ed.
7. Howell. In an American Text-book of Physiology, 1900 ed.
8. Haldane and Smith. (1) Journal of Physiol., XXII, 232. (2) *Ibid.*, XXV, 331. (3) Trans. Path. Soc., Lond., 1900, II.
9. Cabot, R. C. Clinical Examination of the Blood, 1904 ed.
10. Tillmans. Text-book of Surgery, 1901, I, 465.
11. Howell. *Loc. cit.*, No. 7.
12. Vierordt. Anat., physiol., u. physikal. Daten u. Tabellen. Jena, 1893.
13. Hayem. Traitement du choléra. Bull. de Thérap., 1882.
14. Stewart. *Loc. cit.*, No. 6.
15. Taylor and Frazier. The Restitution of the Blood Plasma following Intravenous Saline Injections after Hemorrhage. Univ. Pa., Contrib. Wm. Pepper Lab., 1900, 356–67.
16. Hall and Eubank. The Regeneration of the Blood. Jour. Exper. Med., N. Y., 1896, I, 656–76.
17. Cabot. *Loc. cit.*, No. 9.
18. Schmalz. Pathologie des Blutes. Leipsic, 1896.
19. Yarrow. Univ. Med. Mag., 1898.
20. Jones. Jour. of Physiol., 1891, XII, 299.
21. Howell. *Loc. cit.*, No. 7.
22. Howell. *Ibid.*

23. Wright, A. E. A Note on Certain Improvements in the Method of Determining the Condition of Blood Coagulability for Clinical and Experimental Purposes. Brit. Med. Jour., 1894, I, 57.
24. Cabot. *Loc. cit.*, No. 9.
25. v. Mikulicz. Ueber den Hämoglobingehalt bei chirurgischen Erkrankungen mit besonderer Rücksicht auf den Wiederersatz von Blutverlusten. Wien. med. Wochenschr., 1890, XL, 803.
26. v. Bierfreund. Same title as No. 25. Verhandl. d. Deuts. Gesellsch. f. Chir., 1890, XIX, pt. 2, 159–221.
27. Kiefer, G. L. A Study of the Blood after Hemorrhage and a Comparative Study of Venous and Arterial Blood with Reference to the Number of Corpuscles and the Amount of Hemoglobin. Med. News, N. Y., 1892, LX, 225–7.

Chapter IV

28. Malliotis, D. Les troubles visuels graves àpres les pertes du sang. Paris Thesis, 1898.
29. Proell. Sehstörungen nach Blutverlust. Med. Klin., Berlin, March 29, 1908. Abstracted in Jour. Amer. Med. Assoc., 1908, L, 1463.

Chapter V

30. Kinnicutt, F. P. A Contribution to Hemophilia, with Special Reference to the Joint Symptoms of the Disease. Med. Rec., N. Y., 1905, LXVII, 880–6.
31. Weber. See Stempel, *loc. cit.*, No. 36.
32. Townsend. *Ibid.*
33. Muller. *Ibid.*
34. Bates. *Ibid.*
35. Grandidier, L. Die Hämophilie oder die Bluterkrankheit. Leipsic, 1855, 158 p.
36. Stempel, W. Die Hamöphilie; Sammelreferat nach den Arbeiten der Jahre 1889 bis Ende 1899. Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 100, III, 721; 753; 785; 817.
37. Otto. See Stempel, *loc. cit.*, No. 36.
38. Muir, J. Eight Generations of Hemophilia in South Africa. So. African Med. Rec., Cape Town, 1906, IV, 300–2.
39. Weil, P. E. L'hémophilie, pathogénie et sérothérapie. Presse méd., October 18, 1905.

40. Sahli, H. Ueber das Wesen der Hämophilie. Zeitschr. f. klin. Med., 1904–5, LV–LVI, 264–315.
41. Sahli. *Ibid.*
42. Cabot. *Loc. cit.*, No. 9, page 405.
43. Wright, A. E. On a Method of Determining the Condition of Blood Coagulability for Clinical and Experimental Purposes and on the Effect of the Administration of Calcium Salts in Hemophilia and Actual or Threatened Hemorrhage. Brit. Med. Jour., 1893, II, 223–5.
44. Rosner. See Stempel, *loc. cit.*, No. 36.
45. Coe, J. W. The Treatment of Purpuric Conditions and Hemophilia. Jour. Am. Med. Assoc., 1906, XLVII, 1090–3.
46. Grandidier. *Loc. cit.*, No. 35.
47. Eröss. See Stempel, *loc. cit.*, No. 36.
48. Gocht. *Ibid.*
49. Weil. *Loc. cit.*, No. 39.
50. Fischer, H. See Stempel, *loc. cit.*, No. 36.
51. v. Limbeck. *Ibid.*
52. Berggrün, E. Ein Fall von hämorrhagischer Diathese mit Hirnblutung. Arch. f. Kinderheilk., Stuttg., 1896, XXI, 84–8.
53. Janeway, E. G. Med. Rec., N. Y., 1905, LXVII, 913.
54. Stempel. *Loc. cit.*, No. 36.
55. Vickery, H. F. Hemophilia. Boston Med. and Surg. Jour., 1897, CXXXVI, 226–8.
56. Sümmers. See Stempel, *loc. cit.*, No. 36.
57. Sahli. *Loc. cit.*, No. 40.
58. Kinnicutt. *Loc. cit.*, No. 30.
59. Gage, G. C. Hemostatic Effect of Hydrogen-peroxide as Shown in Two Cases of Hemophilia. N. Y. Eye and Ear Infirm. Rep., 1898, VI, 119–21.
60. Davies, R. T. E. Treatment of Hemophilia. Brit. Med. Jour., 1899, I, 339.
61. Broca. Hémostase chèz les hémophiles. B. et M. Soc. de Chir. de Paris, 1907, N. S., XXXIII, 311.
62. Coe. *Loc. cit.*, No. 45.
63. Jones, C. R. Liquor Thyroidei in Hemophilia. Brit. Med. Jour., 1900, II, 1375.
64. Fuller, E. A New Use for Thyroid Extract; a Cure or at least a Complete Control of Hemorrhage through its Administration; its Effect Also on Another Form of Hemorrhage. Med. News, N. Y., 1903, LXXXII, 385–6.

65. Weil, P. E. Des injections des sérums sanguins frais dans les états hémorrhagiques. B. et M. Soc. méd. d. Hop., January 24, 1907.
66. Hayem. De la transfusion du sang considerée comme moyen hémostatique. Gaz. hebd. d. méd. et d. Chir., 1884, XXI, 74–5.
67. Weil. *Loc. cit.*, No. 65.

Chapter VII

68. Oré, P. C. Études historiques, physiologiques, et cliniques sur le transfusion du sang. Paris, 1876, 704 p.
69. Guérin, A. La communauté de circulation. In Lapeyrère, B. J. Notes d'un journaliste. Paris, 1875, 92–7.

Chapter IX

70. Hawk and Gies. The Influence of External Hemorrhage. Am. Jour. of Physiol., XI, 171.

Chapter X

71. Vitzou, A. N. Nouvelles recherches sur la sécrétion interne des reines. Cong. Internat. de Méd., Comptes rend., Paris, 1900, Sect. de Physiol., 131–8.
72. Chatin and Guinard. De la sécrétion interne du rein; exposé théorique et contribution expérimentale. Arch. d. Méd. expér. et d'anat. Path., 1900, XII, 137–58.
73. Lavis, M. A. Recherches expérimentales et cliniques sur la pathogénie de l'urémie. Sécrétion interne des reines et cytotoxines. Lyon, 1905. 290 pp.

Chapter XI

74. Haldane. In Hale White's Pharmacology, *q. v.*
75. Kühne, W. Verfahren bei Vergiftungen durch Kohlenoxid. Centralbl. f. d. med. Wissensch., 1864, II, 134–6.

Chapter XII

76. Wehr. Centralbl. f. Chir., 1888, No. 24.
77. Smith and Washbourn. (1) Trans. London Pathol. Soc., 1897, XLVIII; (2) Brit. Med. Jour., 1898, II; (3) Edinb. Med. Jour., January, 1900.
78. Loeb. Virch. Arch., 1902, CLXVII.

79. STICKER. Zeitschr. f. Krebsforsch., 1904, I.
80. GAYLORD and CLOWES. Surg., Gyn., and Obstet., June, 1906.
81. BASHFORD. Scientific Reports on the Investigations of the Imperial Cancer Research Fund, No. 2.
82. EHRLICH. Experimentelle Carcinomstudien an Mäusen. Arbeiten a. d. Kgl. Inst. f. Exp. Therapie, 1906.
83. CLOWES and BAESLACK. Med. News, N. Y., Nov. 18, 1905.
84. NOVINSKY. Referred to in STICKER'S article in Langenbeck's Klin. Chir., LXXVIII, 774.
85. WEHR. *Loc. cit.*, No. 76.
86. DUPLOY and CAZIN. Bericht des XI Intern. Med. Cong., Rome, 1894.
87. GEISSLER. Verhandl. d. Deuts. Gesellsch. f. Chir., 1895, Berlin, XXIV Cong.
88. SMITH and WASHBOURN. *Loc. cit.*, No. 77.
89. WHITE, POWELL. Brit. Med. Jour., July, 1902.
90. SANFELICE. Centralbl. f. Bakteriol., Parasitenkund. u. Infectionskrank., 1904, XXXVI.
91. STICKER. *Loc. cit.*, No. 79.
92. BASHFORD, MURRAY, and CRAMER. *Loc. cit.*, No. 81.
93. BEEBE and EWING. Jour. of Med. Research, 1906, XV.
94. EWING. From an unpublished research.

CHAPTER XIII

95. HASSE. Ueber das Operations-Verfahren bei der directen Thierblut-Transfusion. Verhandl. d. Deuts. Gesellsch. f. Chir., Berlin, 1874, III, Pt. II, 110; 115.
96. HASSE. *Ibid.*
97. SANDER. See ORÉ, *loc. cit.*, No. 68.
98. THURN. Directe Lammblut-Transfusion. Berl. klin. Wochenschr., 1874, XI, 393.
99. KLINGELHÖFER. See ORÉ, *loc. cit.*, No. 68.
100. BRUGELMAN. *Ibid.*
101. PONFICK. Experimentelle Beiträge zur Lehre von der Transfusion. Arch. f. Path. Anat., 1875, LXII, 273–335.
102. LANDOIS. Zur Statistik und Experimental-Erforschung der Transfusion. Wien. med. Wochenschr., 1868, XVIII, 1693–5.
103. HAYEM. *Loc. cit.*, No. 66.
104. EHRLICH and MORGENROTH. Ueber Hämolysine. Berl. klin. Wochenschr., 1901, XXXVIII, 251–7, and 1900, XXXVII, 681–7.

105. HUNTER, W. The Duration of Life of Red Blood-corpuscles after Transfusion in its Bearing on the Value of Transfusion in Man. Brit. Med. Jour., 1887, I, 192–200.
106. GOLGI and RAGGI. Quoted from GIRARD, N. Jour. méd., Paris, 1880, I, 185–7.
107. SCHULTZ. Bleibt artgleicher Blut bei der Transfusion erhalten? Deuts. med. Wochenschr., 1905, XXXI, 285.
108. HUNTER, W. Summary of Three Lectures on Transfusion; its Physiology, Pathology, and Practice. Brit. Med. Jour., 1889, II, 116; 237; 305.
109. DIEULAFOY.—Étude sur la transfusion du sang dans la maladie de Bright. Gaz. hebd. de méd., 1884, 2s., XXI, 37–40.
110. HUNTER. *Loc. cit.*, No. 108.
111. HAYEM. *Loc. cit.*, No. 4.
112. JENNINGS. Transfusion, etc. London, 1883. 102 pp.
113. MORTON, T. G. Transfusion of Blood and its Practical Application. In a "Series of American Clinical Lectures," N. Y., 1879.
114. ORÉ. *Loc. cit.*, No. 68.
115. SENN, N. An Experimental and Clinical Study of Air Embolism. Annals of Surgery, 1885, I, 517–49.
116. MARTIN. Entrance of Air into Veins. Internat. Med. Mag., 1892, II, 1033–40.
117. ROUCHOUX. Cited by MARTIN, *loc. cit.*, No. 116.
118. HERTWIG. *Ibid.*
119. FANEY. Du traitement des hémorrhagies par le sérum salé. Paris Thesis, 1896.
120. ORÉ. *Loc. cit.*, No. 68.
121. MAGENDIE. Sur l'entrée accidentelle de l'air dans les veines. Jour. de Physiol. Expériment., 1821, I, 190–6.
122. SENN. *Loc. cit.*, No. 115.
123. ORTH. See HUNTER, *loc. cit.*, No. 131.
124. TILLMANS. *Ibid.*
125. HINDENLANG. *Ibid.*
126. WORM-MÜLLER. *Ibid.*
127. BAREGGI, C. Sull'injezione Ipodermica di Sangue; Esperienze Fisiologiche e Cliniche. Gazz. d. Osp., Milano, 1881, II, 1005–61.
128. PENZOLDT. See HUNTER, *loc. cit.*, No. 131.
129. WINTRICH. *Ibid.*
130. CORDUA. Ueber den Resorption-Mechanismus von Blut-Ergüssen. Berlin, 1877.

131. Hunter, W. Intraperitoneal Blood-transfusion, and the Fate of Absorbed Blood. Jour. Anat. and Physiol., Lond., 1886–7, XXI, 138; 264; 450.
132. Obalinski. Jahresber. f. d. gesam. Med., 1889, 315.
133. Maas. Ueber Intraperitoneale Bluttransfusion bei Thieren. Königsburg i. P., 1881. In-Dis.
134. Grenet, A. Des injections de sang dans la cavité péritonéale. Paris Thesis, 1883.
135. Hayem. De la transfusion péritonéale. C. R. Acad. de Sciences, 1884, XCVIII, 749–51.
136. Golgi and Raggi. *Loc. cit.*, No. 106.
137. Corona and Loco-Pisani. Centralbl. f. Chir., 1883, XXIII, 599.
138. Howe, J. W. Experiments in Peritoneal Transfusion. Med. Rec., N. Y., 1883, XXIII, 120–2.
139. Ledderhose, G. Beiträge zur Kenntniss des Verhaltens von Blutergüssen in serösen Höhlen. Strassburg, 1885, p. 108.
140. Howe. *Loc. cit.*, No. 138.
141. Wintrich. See Hunter, *loc. cit.*, No. 131.
142. Golgi and Raggi. *Loc. cit.*, No. 106.
143. Southgate, T. H. Blood Absorption from the Peritoneal Cavity. Med. Rec., N. Y., 1895, XLVIII, 221.
144. Hunter. *Loc. cit.*, No. 131.
145. Obalinski. *Loc. cit.*, No. 132.
146. Maas. *Loc. cit.*, No. 133.
147. Corona and Loco-Pisani. *Loc. cit.*, No. 137.
148. Golgi and Raggi. *Loc. cit.*, No. 106.
149. Wegner. Arch. f. klin. Chir., 1877, XX, 85.
150. Ledderhose. *Loc. cit.*, No. 139.
151. Hunter. *Loc. cit.*, No. 131.
152. Dubar and Remy. Sur l'absorption par le péritoine; notions anatomiques et physiologiques tirées de la recherche des voies parcourues par les substances absorbées dans l'animal vivant. Jour. de l'anatomie et physiol., Paris, 1882, XVIII, 60, 342.
153. Starling and Tubby. On Absorption from and Secretion into the Serous Cavities. Jour. of Physiol., 1894, XVI, 140–55.
154. Grenet. *Loc. cit.*, No. 134.
155. Southgate. *Loc. cit.*, No. 143.
156. v. Recklinghausen. Centralbl. f. Med. Wissensch., 1867, No. 31.
157. Hayem. *Loc. cit.*, No. 135.
158. Kolossow. Arch. f. Mikroskop. Anat., 1894.
159. Muscatello. Virch. Arch., 1895, CXLVIII, 327.

160. HUNTER. *Loc. cit.*, No. 131.
161. HAYEM. *Loc. cit.*, No. 135.
162. LEDDERHOSE. *Loc. cit.*, No. 139.
163. HOWE. *Loc. cit.*, No. 138.
164. CORONA and LOCO-PISANI. *Loc. cit.*, No. 137.
165. LANDERER. Virch. Arch., 1886.
166. MOSLER. Deuts. Arch. f. klin. Chir., 1881, XXVIII, 476.
167. KARST. Injectionen von Defibrinirten Blute ins Unterhautbindgewebe. Berl. klin. Wochenschr., 1873, X, 587.
168. LANDENBERGER. Zur subkutanen Injection von defibrinirten Thierblut bei Kranken. Med. Corresp.-Blatt. d. Württem. ärztl. Vereins, 1874, XLIV, 260–1.
169. JULLIEN, L. De la transfusion du sang. Paris, 1875.
170. PONZA, G. L. La Trasfusione Sottocutanea. Morgagni, Napoli, 1875, XVII, 753–5.
171. v. ZIEMSSEN, H. Lecture on Subcutaneous Blood-injections, Salt Water Infusion, and Intravenous Transfusion. Jour. Amer. Med. Assoc., 1887, IX, 35–9; 68–72.
172. LANDENBERGER. *Loc. cit.*, No. 168.

CHAPTER XIV

173. QUEIROLO. Moleschott. Untersuch., 1895, XV, 228–40.
174. PAYR. Beiträge zur Technik der Blutgefässe und Nervennaht nebst Mittheilungen über die Verwendung eines resorbibaren Metalles in der Chirurgie. Arch. f. klin. Chir., 1900, LXII. See also, Weitere Mittheilungen über Verwendung des Magnesiums bei der Naht der Blutgefässe, *ibid.*, 1901, LXIV, 726–40.

CHAPTER XV

175. DEBOVE and BRUHL. Des élévations de température produites par les injections sous-cutanés de sérum artificial. B. and M. Soc. Méd. d. Hop. d. Par., 1895, 3s., XII, 270–3.

CHAPTER XVI

176. METCHNIKOFF, E. L'immunité dans les maladies infectieuses. Paris, 1901, p. 600.
177. GENGOU. Sur les sensibilisatrices des sérums actifs contre les substances albuminoïdes. Annales de l'Inst. d. Pasteur, 1902, XVI, 734.

178. Hektoen, L. Isoagglutination of Human Corpuscles with Respect to Demonstration of Opsonic Index and Transfusion of Blood. Jour. Amer. Med. Assoc., 1907, XLVIII, 1739–40.
179. Landsteiner. Quoted by Hektoen. See, Ueber Serumagglutinine. Münch. med. Wochenschr., 1902, XLIX.
180. Descatello and Sturli. Quoted by Hektoen, *loc. cit.*, No. 178.

Chapter XVII

181. Bell and Osler. Case of Progressive Pernicious Anemia. Trans. Canad. Med. Assn., 1877, I, 131–40.
182. Kahler, O. Beobachtungen über progressive perniciöse Anämie. Prag. med. Wochenschr., 1880, V, 373–5 *et seq.*
183. Brakenridge, D. J. Transfusion of Human Blood in the Treatment of Pernicious Anemia. Edinb. Med. Jour., 1892–3, XXXVIII, 409–29.

Chapter XVIII

184. Andrew and Callender. Leukemia Treated by Transfusion of Defibrinated Blood. St. Barth. Hosp. Rep., 1873, IX, 216–20.
185. Mosler, F. Transfusion bei Leukämie. Berl. klin. Wochenschr., 1866, III, 197–201.
186. Gallaher. A Case of Leucocythemia with Great Exhaustion following Diarrhea; Transfusion of Human Blood; Death. N. Y. Med. Jour., 1875, XXII, 395–8.

Chapter XXIII

187. Barwell, R. On Transfusion of Blood in Chronic Anemia following Injury. Lancet, 1877, I, 312, American edition.

Chapter XXV

188. Mosler, F. Ueber arterielle Transfusion defibrinirten Menschenblutes bei Darmblutung im Verlaufe von Typhus abdominalis. Berl. klin. Wochenschr., 1875, XII, 265–8.
189. Stone. A Successful Case of Transfusion after Grave Hemorrhage in Typhoid Fever. Northwest Lancet, St. Paul, 1882–3, II, 264–5.
190. Gibert. Observation de transfusion du sang dans un cas de fièvre typhoïde grave compliquée d'hémorrhagie intestinale. Bull. Acad. de Méd., Paris, 1881, 2s., X, 419.

191. WHITWELL, W. S. Report of a Case of Successful Transfusion in Typhoid Fever. Pacific Med. and Surg. Jour., 1886, XXIX, 193–8.

192. DARÈNE, J. B. Étude sur la transfusion du sang à la suite des hémorrhagies intestinales survenant dans le cours de la fièvre typhoïde. Paris Thesis, 1882.

193. MAHOMED, F. Two Cases of Direct Transfusion of Blood for Hemorrhage in Typhoid Fever. Lancet, 1881, II, 950.

194. PEPPER and NISBET. A Case of Fatal Hemolysis following Direct Transfusion of Blood by Arteriovenous Anastomosis. Jour. Amer. Med. Assoc., 1907, XLIX, 385–9.

195. STOKES. Transfusion Successfully Performed on a Child (for Typhoid Hemorrhages, Author). Trans. Phila. Obst. Soc., 1878, V, 10–14.

196. BOISNOT, J. A Case of Purpura Hemorrhagica Requiring Transfusion. Phila. Med. Times, 1875, V, 371–3.

197. LANE, S. Hemorrhagic Diathesis. Successful Transfusion of Blood. Lancet, 1840, 185–8.

198. WATTS. Johns Hopkins Hosp. Bull., May, 1907.

199. MICHEL, C. Transfusion mit Erfolg nach einer profusen Magenblutung bei einem 63-jährigen Manne. Berl. klin. Wochenschr., 1870, XLIX, 591–2.

200. BREWER. From a private communication.

CHAPTER XXVI

201. LÖWENTHAL, S. Ein Fall von Bluttransfusion bei Leuchtgasvergiftung. Wien. klin. Wochenschr., 1892, V, 378–80.

202. HALSTEAD, W. S. Refusion in the Treatment of Carbonic Oxide Poisoning. Ann. of Anat. and Surg., January, 1884.

203. JERSEY. Cited by BULL. N. Y. Med. Rec., 1884.

204. WILKIE. *Ibid.*

205. SCHRUBER. *Ibid.*

206. VON GORDON. *Ibid.*

207. PILCHER. Illuminating Gas Poisoning. Brooklyn Med. Jour., May, 1903.

208. STOCKER, S. Die Transfusion bei Kohlendunstvergiftung. Correspondenzbl. f. Schweiz. Aertze, 1888, XVIII, 258–61.

209. LÖWENTHAL. *Loc. cit.*, No. 201.

210. PILCHER. *Loc. cit.*, No. 207.

211. HÜTER, C. Fall von Kohlenoxydvergiftung. Berl. klin. Wochenschr., 1870, XXVIII, 341.

212. Samuelson. Fall von Transfusion bei Kohlendunstvergiftung. Berl. klin. Wochenschr., 1875, XXXVIII, 525.

213. Lühe. Transfusion bei Kohlenoxidvergiftung mit günstigem Ausgang. Deut. mil.-arztl. Zeitschr., 1878, VII, 263–7.

214. Uterhart, C. Rasche Heilung einer Kohlenoxidgasvergiftung durch die Transfusion. Deuts. Klinik, 1867, XIX, 130.

215. Riedinger. Fall von Kohlenoxidgasvergiftung mit nachfolgender Transfusion und lethalem Ausgang. Chir. klin. im K. Julius Hosp. zu Würzb., 1877–8, 78–80.

216. Garrigues, H. J. Transfusion in Gas Poisoning. N. Y. Med. Jour., 1883, XXXVII, 232–3.

217. Vleminckx, V. Empoisonnement par le vapeur de charbon; transfusion du sang. Bull. Acad. Roy. d. Med. d. Belge, 1876, 3s., X, 106–25.

Chapter XXVII

218. Lange, W. Ein Fall von puerperaler Eklampsie in welchem die Transfusion angewandt wurde und Genesung erfolgte. Vtljschr. f. d. prakt. Heilk., 1868, C, 168–78.

219. Watts. *Loc. cit.*, No. 198.

INDEX

INDEX

THE END